The Journal of
TROPICAL PEDIATRICS

Devoted to all problems of Child Health in
Sub-tropical and Tropical Countries of the World.

VOL. 2. No. 4. MARCH, 1957 PRICE 5/- ($0.70)

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PREPAID SUBSCRIPTION RATES : Per Annum (4 issues) £1 1s. 0d. ($3.20) post free. Single copies 5/3 ($0.80) each, post free.

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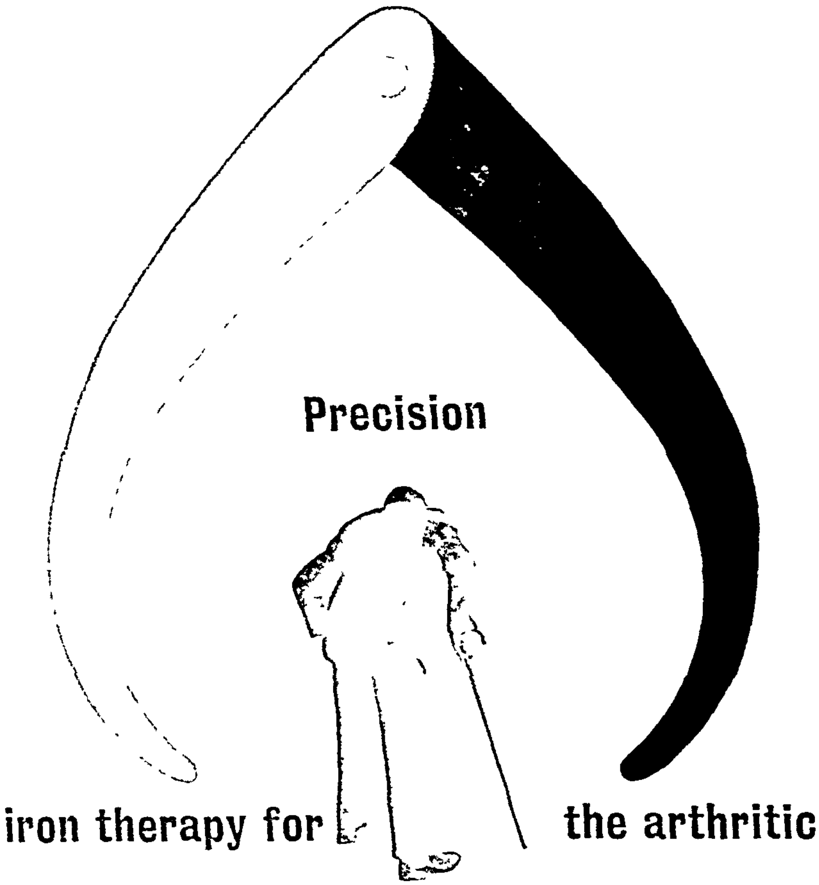
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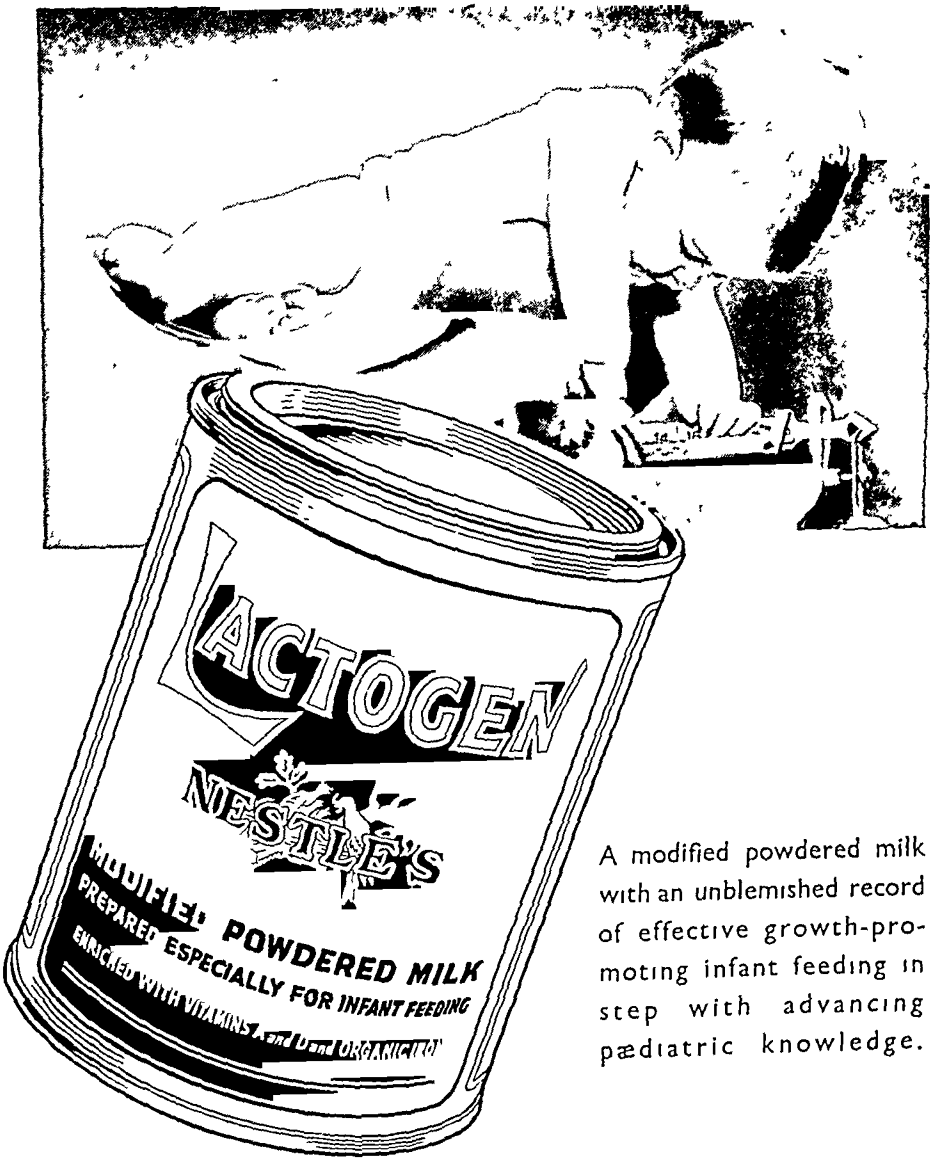
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The Journal of
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EDITORIAL

THE GEOGRAPHICAL PATHOLOGY OF DENTAL CARIES

Dental caries is of worldwide distribution and palaeopathological investigations have shown that the disease has affected man from remotest antiquity.

The present-day high incidence of caries in many countries is a source of anxiety to child health workers, and the geographical pathology of this condition has a dual significance. Firstly, because there is evidence that the condition appears to be occurring more frequently in some tropical areas than previously, and secondly, because a broad-based type of approach may perhaps supply further clues as to etiology of the disease as a whole.

Surveys into the incidence of dental caries in different socio-economic groups in different regions of tropical countries are being undertaken with increasing frequency, but much further information is still needed. Ideally, this type of investigation could most properly be carried out by the dentist, with his specialised skills and techniques ; but, if, as is common, no such facilities are available, valuable results can be obtained by the pediatrician, who can at least, report the D.M.F. (decayed, missing, filled) index (although, in the absence of dental conservation found in many tropical regions, this may well be rather a decayed-missing index).

A survey of the incidence of dental caries, as assessed by straight-forward inspection without the use of a dental probe or mirror, has recently been carried out in Uganda by WELBOURN, when she found 16-20 per cent. of Baganda children of nursery school age to be affected. The upper incisors were especially involved ; while there was evidence that the disease appeared to be increasing in frequency in this group in Uganda, as was suggested by the contrast often noted been the good teeth of mothers and the decayed teeth of their offspring.(1)

That the incidence of dental caries can vary considerably within even a limited geographical area has been indicated by recent surveys in Jamaica. In one rural region 86.8 per cent. of village children were found to have caries(2) ; by contrast, more recently Back, as a part of a survey of small farmers all over the island, found only 7 per cent. of children aged between three and 13 years to have more than 4 carious or missing teeth, while, at the same time, he stressed the considerable variation noticed from one district to another.(3)

In Asia, Finn has recently surveyed the literature on the status of caries in China, Tibet, Malaya, Mongolia, India and the Philippines(4) ; while Kridakara et al. have reported the results of a survey in Thailand, when it was found that the condition was commoner among children in Bangkok than among these living in the rural, more traditional town of Chiengmai, possibly as a result of the greater consumption of sugar and wheat flour among the former.(5)

If, as appears certain, dental caries is in fact, becoming a problem in tropical children, it is then necessary to consider appropriate health teaching for clinics and schools. This will have to be as simple as possible and based both on a knowledge of local facilities and present practices, which should be retained if desirable or adapted when feasible. Basically, it would seem that, apart from measures aimed at improving the general nutrition, three types of practical advice can be considered — firstly, the avoidance of foods made of refined sugar and overmilled flour, especially between meals ; secondly, the desirability of cleaning the teeth, especially at night ; and, thirdly, the possibility of rinsing out the mouth with water after meals — a practice already used by Hindus. Whether a toothbrush or the local equivalent, usually a tooth-stick, should be advised for cleaning the teeth will have to be considered.

Finally, it must be stressed that, in surveys of the incidence of dental caries, other aspects of oral pathology should be observed, including the presence of dental calculus and disease of the gums, including marginal gingivitis and pyorrhoea.

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A FIVE YEAR FOLLOW-UP OF COLOURED CHILDREN WITH KWASHIORKOR IN CAPE TOWN

by

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(Departments of Child Health and Pathology, Groote Schuur Hospital, and University of Cape Town)

We report here a follow-up study of 27 cases of kwashiorkor in Coloured† children in Cape Town. They were part of a group of 90 cases seen by one of us, and clinical accounts of them will be published and have already been recorded (SUCKLING, 1955). No study comparable to this seems to have been reported.

Of the 90 cases, 50 were male and 40 female. Thirty-one died at the time of their original illness (13 male and 18 female). Of the remaining 59 it has been possible to follow-up 27 on one or more occasions (Table I). One child is known to have been drowned, one has left the district and one has tuberculous hip disease. The age of the subjects is shown in the table.

These patients conform to descriptions of kwashiorkor given elsewhere in Africa, with allowance for the fact that the Coloured people are not so deeply pigmented as the Bantu. Similar cases here have been accepted for metabolic study by BROCK (BROCK *et al.*, 1955) as typical examples of this type of protein malnutrition. All the children of our series were oedematous and hypoalbuminaemic. Sixty per cent. showed skin and mucous membrane changes of the type seen in kwashiorkor. In fifteen per cent. the liver was enlarged.

The initial observations on our patients were in complete accord with the criteria on which a diagnosis of kwashiorkor must rest and the early progress, in the fifty-nine who recovered, followed the recognized pattern. Many investigators have traced in

TABLE I. Ages of twenty-seven cases of kwashiorkor on admission and at follow-up.

Age of patients at admission and follow-up examinations			
	Admission	Follow-up 1952	 1955
Number of cases	27	23	24
Mean age (months)	15.90	40.10	73.38
Standard deviation	4.00	5.05	7.87

---

* We are grateful to Dr. Wolf Rabkin, lately physician-in-charge of the Paediatric Department, and Professor F. J. Ford, Professor of Child Health, for permission to study patients under their care.

Professor J. F. Brock, Professor J. G. Thomson and Dr. J. D. L. Hansen gave constant encouragement and advice.

The difficult task of following-up patients was made possible by the services of Miss A. Moodie, Medical Social Worker attached to the Research Unit in Clinical Nutrition maintained by the Council for Scientific and Industrial Research under the direction of Professor Brock.

† The Coloured race is derived from a mixture of European with Malay, Hottentot, Bantu and Bushman stock. Their way of life is patterned on the European rather than the Bantu.

detail the changes during the convalescent stage of the disease, but remarkably little is known of the subsequent course of events. The difficulties involved in a long-term study of the type of family to which these children belong are, even in socially-advanced countries, considerable. With us they are formidable and account for the failure to maintain contact with such a high proportion of our patients.

Two follow-up examinations were made at approximately 2 and 5 years after the original admission. A clinical assessment was made, and in the majority the haemoglobin content of the blood was estimated and a liver biopsy done. At the same time a social worker visited the home and supplied a report on the conditions there.

SOCIO-ECONOMIC FACTORS

Poverty is the rule in the Coloured people, and cases of kwashiorkor are found among the poorest of them (Table II). The homes of all classes have been visited at the time of both follow-up examinations, and the story is a monotonous one of miserable living conditions and an indeterminate diet. Table II shows the general financial status of these people and the comparable figures for the families of our kwashiorkor patients.

TABLE II. Distribution of Coloured households on the Cape Flats (the Cape isthmus) in relation to the Poverty Datum Line (P.D.L.).

Sample	Below P.D.L.	Between P.D.L. and twice P.D.L.	Above twice P.D.L.	Total
Cape Flats Survey dated 9/6/53 (A)	347	250	73	670
As percentage of sample	52	37	11	
This series (B) (all cases)	37	8	0	45
As percentage of sample	82	18	0	

The Poverty Datum Line is calculated on the current cost-of-living index, and different money requirements are laid down for individual members of a household. If the total income does not reach this figure, the household is considered to be below the P.D.L. The figures for series (A) are taken from a sociological study conducted by BATSON. The series (B) noted here includes all the cases in our own series for whom it was possible to calculate the P.D.L. and is not confined only to follow-up cases.

It was often impossible to obtain the necessary information either because the mother left the hospital or because the home could not be found. It is obvious that, in this type of community (Sample A), rather more than half of the families have an extremely meagre existence and that in the presence of kwashiorkor in the children the socio-economic background (Sample B) is even worse.

Under these circumstances it is very surprising to note that, of the original 59 cases who survived, only 2 were readmitted (one on two occasions) for a recurrence of the disease. These re-admissions took place on each occasion three months after discharge from hospital. In the series which was followed up only one family is known to have had subsequent children affected, and in this instance the mother has had four more children in five years and all are said to have been oedematous, presumably due to protein malnutrition. The reason for the low recurrence rate will be referred to later.

CLINICAL FEATURES

The World Health Organisation (BROCK and AUTRET, 1952) list ten dominant, even fundamental, disturbances making up the syndrome of kwashiorkor. Certain of these are transitory and disappear within 1-3 weeks on a skimmed milk diet.

In Cape Town it has been found that the oedema disappears in 7-10 days, unless there is a concomitant tuberculous infection, when it may last longer. The serum albumen also rises rapidly and in about a fortnight returns to the normal limits for the age. The dermatosis is well on the way to recovery in a week though the characteristic areas of depigmentation remain longer.

Diarrhoea, almost always present, responds quickly to diet and antibiotics, though the stools may remain loose for 3-4 weeks. The peevishness and mental apathy are replaced by a happy temperament in 2-3 weeks. If E.C.G. changes are present (SUCKLING, 1955), correction of electrolyte deficiencies is accompanied by a rapid change towards normality, and the E.C.G. is completely normal within a month.

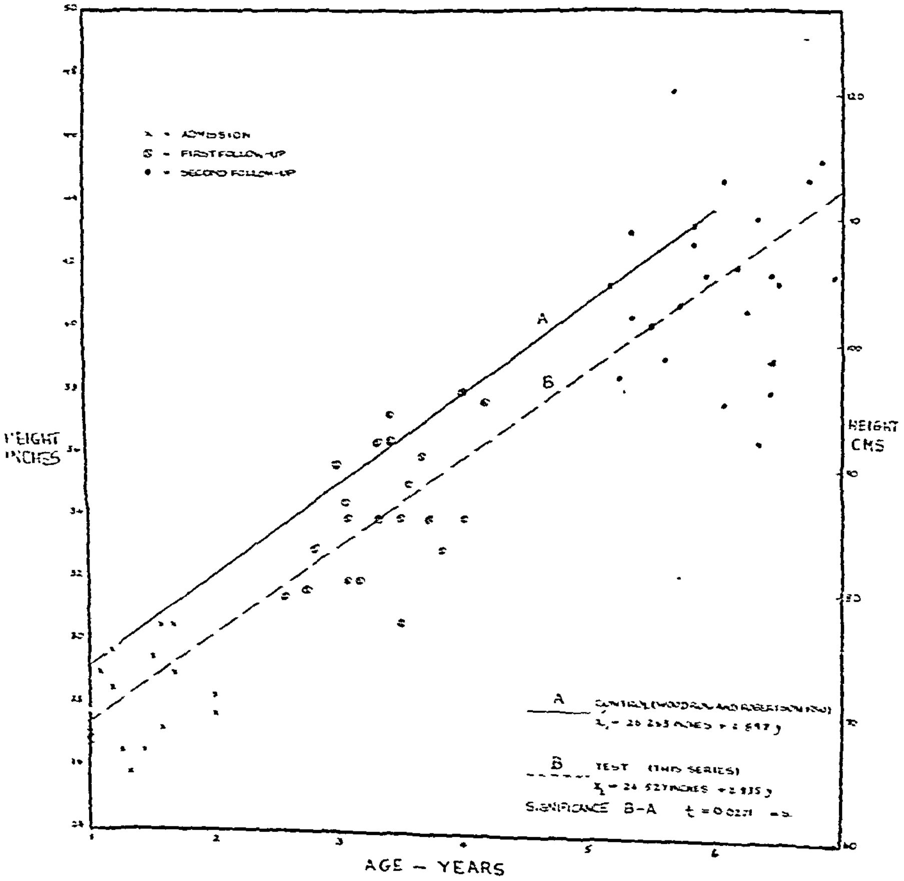

FIG. 1. Height (Recumbent).

At follow-up examinations the general health of the children was good. Though small for their age, they appeared normally built, and of good intelligence. They were active and cheerful. At the 1952 follow-up, one child was found to have primary tuberculosis. No case was found with hepatomegaly, nor skin, nor hair, nor mucous membrane changes of nutritional origin.

In 1955 another case of primary tuberculosis was found. Five children had skin or mucous membrane changes, which appeared to be of nutritional origin. One boy was found to have a liver enlarged to two fingers breadths below the costal margin in the right anterior axillary line, and it felt unduly firm and the edge irregular. There was no splenomegaly nor distension of the abdominal veins. The serum albumen was 4.9 gm. per cent. and the globulin 3.3 gm. per cent. The thymol turbidity test was 4 units and the thymol flocculation 2 units, so that the liver function tests were slightly abnormal. It was confidently expected that the needle biopsy would show some abnormality, but the liver parenchyma was normal, and there was no evidence in that specimen of liver fibrosis. It is of interest that at the original admission this child had a liver enlarged to 3 fingers breadths, which persisted for 3 weeks until choline chloride was given. Within a week of this treatment the liver had receded above the costal margin. On the original admission the plasma proteins were 3.41 gm. per cent. and the prothrombin time (Quick's one stage) 85 per cent. normal. The Wasserman and Van der Bergh reactions were negative. It is also of interest that when this boy was examined in 1952 the liver was

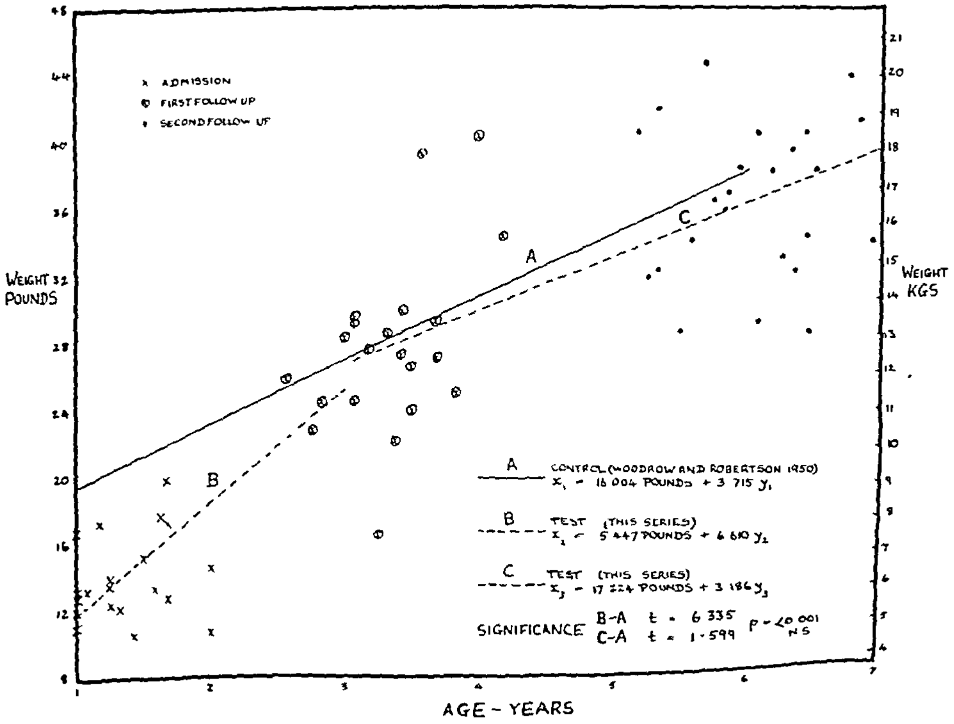

FIG. 2. Weight.

noted as " normal." It must be stressed that this child is the exception and the cause of the enlarged liver remains obscure. It has not yet been possible to investigate him further. No other case of hepatomegaly was seen.

At neither follow-up was any child oedematous nor was any abnormality of the eyes noted.

Dental caries is not uncommon in the Coloured people, but the incidence did not seem to be more than usual in these children, nor to have increased at consecutive follow-up examinations.

It is difficult to define dyspigmentation of the hair in this group owing to their mixed ancestry. A reddish colour is common and normal. Snips of hair were taken at all three examinations and compared with one another, but no conclusions could be drawn. In some cases light hair became dark, and in some cases the reverse was found. Dry, sparse hair was usually found at admission, and there was commonly a patchy alopecia. At both follow-up examinations the hair was normal in texture and distribution.

Anaemia has been recognized as a feature of kwashiorkor in most of the surveys of the disease (BROCK and AUTRET, 1952), and it has been found in this series. In tropical countries the anaemia has not uncommonly been found to be macrocytic in type. Complicating infestations such as hookworm and malaria have, however, made the issue more involved. These diseases are not found in Cape Town, and the anaemia can, therefore, be considered as part of the symptom-complex of kwashiorkor.

The figures for the haemoglobin concentrations are set out in Table III. It will be seen that at the 1952 follow-up an improvement had occurred, and that after five years recovery was complete. On admission the blood films generally showed marked anisocytosis and poikilocytosis, and hypochromia was not uncommon. Only one child showed macrocytosis.

TABLE III. Haemoglobin estimations in cases of kwashiorkor on admission and at follow-up.

Haemoglobin Estimations : (g /100 ml)			
	On admission	Follow-up	
		1952	1955
Number of readings	19	15	21
Mean Hb	10.55 (11.7)*	11.30 (13.3)	13.53 (13.3)
Standard deviation (S D) $\sqrt{\frac{n}{n-1}} \times S\,D$	2.34 (0.8)	1.34 (0.8)	0.97 (0.8)

* Figures in parenthesis are the normal for the age in American children (HOLT, 1953).

The head circumference was normal at admission and at follow-up examinations, when compared with American children (HOLT, 1953). Radiologically the bone age was also within normal limits.

The graphs for height and weight are set out in Figs. 1 and 2. The regression slopes were calculated by Dr. B. BRONTE-STEWART. Individual heights and weights are plotted for this series, and the regression slopes for both this series and the controls (WOODROW and ROBERTSON, 1950). The control series is a highly selected group, whose mothers took the trouble to take them to the Welfare clinics, where they received extra food if necessary.

The "control" regression slopes for both height and weight correspond almost exactly to the regression slope for minus 2½ times the standard deviation for American children (HOLT, 1953). In other words the weight and height regression slopes for the control series of Coloured children are well below the normal for American children.

The regression slope for height does not differ significantly for the control and kwashiorkor series. At one year of age the child with kwashiorkor is, on the average, 2 inches shorter and this difference is maintained but not increased with the passage of time. It is probable that the child with kwashiorkor approximates to the "average" Coloured child, and that the "control" represents a higher social class.

The weight regression slopes are different. It is necessary to have two slopes for the kwashiorkor cases, as a single linear slope cannot be drawn. By the time of the 1952 follow-up the kwashiorkor cases had caught up with the controls, and from the 1952 to the 1955 follow-ups they gained at the same rate. Insufficient readings have been taken to indicate how long the kwashiorkor children take to catch up, but it is probably less than the two years span covered here, between the initial illness and the 1952 check.

It must be stressed that the number of readings is small, not exceeding three for any one child, but the trend seems clear. The rapid recovery in weight may be due to dietary advice given on discharge from hospital, and possibly also to help from Child Welfare clinics, to which all cases were referred.

These children returned from hospital to the environment which had provoked the disease, and the results cannot be considered the best obtainable. The Coloured group is on the whole of short stature and nutritional factors may play a significant part. There is a known tendency for well-nourished races to increase in height.

PANCREATIC DYSFUNCTION

In this series 14 cases underwent duodenal intubation at their first admission, and 7 of them were serially examined. The findings agreed with those of VEGHELYI (1950) in that lipase and amylase contents were greatly reduced or absent, and that trypsin was also reduced, but to a lesser extent. Recovery was rapid and the enzyme concentrations were restored to normal in 3 weeks.

Histological studies were made by one of us (J.A.H.C.) on 38 cases of kwashiorkor which came to autopsy during the period 1950-1955. Sections were available from 35 of these and 29 showed moderate or severe pancreatic atrophy accompanied in one by duct obstruction and fibrosis. In 6 instances the pancreas was normal.

No estimations of duodenal contents were made at follow-up examinations, but there was no story suggestive of steatorrhoea nor clinical evidence of pancreatic dysfunction. It appears likely that in this series there was at the onset pancreatic damage which disappeared completely, possibly in the three weeks after initiation of convalescence during which the stools tended to be frequent and loose.

PATHOLOGICAL FINDINGS FROM LIVER BIOPSIES

Liver biopsies, taken by needle puncture, were available from 25 children. Seventeen were biopsies at the 1952 follow-up (Dr. P. SWANEPOEL), 20 at the 1955 follow-up, and 14 on both occasions. All material was fixed in formol-saline. Frozen sections were stained with Sudan IV, and paraffin sections with haematoxylin and eosin, van Gieson's stain, Best's carmine for glycogen, with the Prussian Blue reaction for free iron, and by silver impregnation methods for reticulum fibres. Control autopsy material was studied from 5 European children, aged 1-3½ years, and from one Coloured child of 11 months.

No child was subjected to liver biopsy when ill and first admitted to hospital, so that we have no proof that they all showed fatty livers at that time. That they did have fatty livers may be presumed in view of biopsy findings in similar cases elsewhere (GILLMAN and GILLMAN, 1945), and from our post-mortem findings in such cases. This is supported by subsequent liver biopsies performed in this hospital on cases of kwashiorkor at the time of their original illness (HANSEN, 1956).

In this department in the period 1950 to 1956, 38 children came to autopsy with the clinical diagnosis of kwashiorkor. Ten of these 38 children formed part of the clinical material reported in this paper. In these 10 autopsies hepatic fatty changes were severe in 5, moderate in 3, slight in one, and absent in one. Post-mortem examination of the remaining 28 children showed severe fatty liver in 23, moderate in 2, slight in 3 and absent in one. Some degree of fatty liver was thus present in 36 of 38 children (95 per cent.) in whom the clinical diagnosis of kwashiorkor was made, and was moderate to severe in 32 of the 38 (84 per cent.). On the basis of this evidence, it is a reasonable assumption that the majority of our liver biopsies came from children who had fatty livers when first admitted to hospital.

Before describing the results of the follow-up liver biopsies, it seems relevant to state that focal necroses were found in 2 of the 38 fatty livers obtained at post-mortem from children diagnosed clinically as suffering from kwashiorkor.

The findings in the follow-up liver biopsies were in striking contrast to the presumed background of abnormality, because the majority were basically normal and those with significant changes were the exception. Severe fatty changes were not seen in any specimen. In 3 instances fat was present in very modest amount in the liver cells, though Kupffer cells alone contained small fat globules in nearly all the specimens.

Free iron pigment was similarly inconspicuous, and it was present in quite trifling amounts in one biopsy only. No liver biopsy showed any of the features described by HILL (1951) as occurring in the serous hepatosis of Jamaican children or of those noted by BRAS *et al.* (1954) in Jamaica in relatively poorly nourished children (" Veno-occlusive disease of the liver ").

The features of cirrhosis were consistently absent, though one child had clinical hepatomegaly at the time of the second liver biopsy. In one section from his biopsy the edges of three portal tracts could not be clearly defined, and silver staining showed periportal reticulum fibres, increased to a degree not seen in the control material. A second biopsy done three years later on this particular child showed a normal picture in all respects, though the specimen was rather a small one. In several sections the number and thickness of reticulum fibres forming the pattern of sinusoids was greater than expected, but not in excess of what was seen in the control material, particularly in subcapsular areas.

Other abnormalities were infrequent and slight, and of doubtful significance. Portal triads showed increased cellularity in 3 biopsies, chiefly in the form of small round cells resembling lymphocytes. The meaning of this finding is not clear, but the excess of cells was not present in biopsies done three years later in 2 of these 3 children. In 4 cases a small minority of the cells were morphologically different from the rest of the glycogenrich liver cells. They were smaller, their cytoplasm was more eosinophilic and their nuclei sometimes denser. It is doubtful what causes these effects but, as similar appearances occur frequently in biopsies from adults and children with a great diversity of lesions, they would not seem to have any special relation to malnutrition, and may well be a form of artefact.

Incidental lesions were present in liver biopsies from 3 children. Two of these showed tubercle follicles and the third glycogen degeneration of periportal nuclei. Both children with tubercle follicles had second biopsies done 3 years afterwards, and these were normal.

The results of the study indicate, therefore, that the liver can recover apparently completely from changes observed in kwashiorkor. They show that the fatty liver, which is almost certainly present in the majority of cases when first admitted to hospital, is not necessarily followed by fibrosis. DAVIES (1954) in Uganda has stated that hepatic fibrosis in kwashiorkor is not directly related to fatty liver. Our experience is in agreement with him on this point, though very different in the incidence of hepatic fibrosis which he found in Uganda children under 5 years of age (DAVIES, 1948).

SUMMARY

(1) Despite a return to the poor surroundings, which encourage the disease, children with kwashiorkor in Cape Town usually make a good recovery.

(2) With correct treatment, quick recovery takes place from oedema, hypoalbuminaemia, skin and mucous membrane changes, pancreatic dysfunction, electrocardiographic changes and disorders of temperament, and there is no evidence of permanent damage.

(3) Growth in height is maintained at the same rate as in controls, and though at a lower level does not differ statistically from those controls. Growth in weight shows that there is recovery in 2 years from the malnutrition found on admission, and that thereafter it progresses at the same rate as the controls.

(4) Anaemia is corrected more slowly, but recovery is complete in 5 years.

(5) Liver biopsies show that the liver does recover completely from the fatty change of kwashiorkor. The histological features of cirrhosis were consistently absent, though one child had suggestive clinical signs. Other microscopic abnormalities in the biopsy sections were infrequent and slight.

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ILLEGITIMACY IN DURBAN.

by

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Illegitimacy is culturally defined. This investigation, therefore, does not purport to be a detailed sociological study, since for that, figures of illegitimacy must be related to the social conditions of the communities represented — their modes of marriage, family structure, religious sanctions, and legal and moral codes; economic standards also influence the incidence of illegitimacy and attitudes towards it.

In Western society illegitimate children are those born out of wedlock, in urban African society marriage rites may be delayed, but children are regarded as legitimate by virtue of the stability of the relationship between parents, or the promise of marriage when economically possible.

MALINOWSKY (1930) in his writings on marriage and kinship stresses the " principle of legitimacy." By this is meant that in all human societies a woman has to be married before she is allowed to conceive. This attitude prevails not only among European but among primitive peoples as well. Even where pre-nuptial intercourse is tolerated, there is no tolerance to conception. He states further " the most important legal rule concerning the physiological side of kinship is that no child can be brought into the world without a man, and one man at that, assuming the rôle of sociological father, that is guardian and protector, the male link between the child and the rest of the community."

KABERRY (1949) queries whether in Australia, where there is no recognition of physiological fatherhood among the aborigines, one can speak of illegitimate children at all. She states that " as a rule a girl was living with her husband at puberty, and since there is no recognition of physical paternity, all the children she bore were regarded as his." MALINOWSKI'S principle of legitimacy is seen in Durban Indians where the desire is not for many children but for many legitimate children.

DATA USED.

Durban offers a fruitful field for a comparative study of illegitimacy, as it has at least four distinct race groups — European, Coloured, Bantu and Indian. Data were

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* This paper forms part of the material of an M.D. Thesis (University of Cape Town).

TABLE I. Age distribution of married and unmarried mothers. Births registered in Durban, 1948.

Age	European				Coloured				Bantu				" Passenger " Indian			
	Married	Unmarried	Total	% Unmarried	Married	Unmarried	Total	% Unmarried	Married	Unmarried	Total	% Unmarried	Married	Unmarried	Total	% Unmarried
14-15	—	—	—	—	—	—	—	—	—	16	16	100 0	1	—	1	0 0
16-17	14	1	15	6 7	4	12	16	75 0	9	220	229	96 1	18	—	18	0 0
18-19	138	—	138	0 0	42	28	70	40 0	80	607	687	88 4	54	2	56	3 6
20-21	335	15	350	4 3	65	42	107	39 3	299	696	995	69 9	60	—	60	0 0
22-23	420	10	430	2 3	53	30	83	36 1	425	604	1029	58 7	73	—	73	0 0
24-25	448	6	454	1 3	68	31	99	31 3	489	428	917	46 7	68	—	68	0 0
26-27	439	4	443	0 9	58	17	75	22 7	408	264	672	39 3	63	—	63	0 0
29-29	370	3	373	0 8	43	14	57	24 6	370	216	586	36 9	58	1	59	1 7
30-31	284	4	288	1 4	35	11	46	23 9	258	115	373	30 8	51	—	51	0 0
32-33	259	2	261	0 8	23	7	30	23 3	171	81	252	32 1	41	—	41	0 0
34-35	193	3	196	1 5	22	5	27	18 5	144	55	199	27 6	32	—	32	0 0
36-37	126	1	127	0 8	23	2	25	8 0	142	45	187	24 1	20	—	20	0 0
38-39	100	3	103	2 9	18	2	20	10 0	145	36	181	19 9	19	—	19	0 0
40-41	65	1	66	1 5	10	1	11	9 1	70	18	88	20 5	4	1	5	20 0
42 43	20	—	20	0 0	6	1	7	14 3	39	10	49	20 4	5	—	5	0 0
44-45	9	—	9	0 0	1	—	1	0 0	13	8	21	38 1	—	—	—	—
46-47	3	—	3	0 0	—	—	—	—	9	5	14	35 7	3	—	3	0 0
48-49	—	—	—	—	—	—	—	—	11	2	13	15 4	—	—	—	—
50 51	1	—	1	0 0	—	—	—	—	2	—	2	0 0	—	—	—	—
	3224	53	3277	1 62	471	203	674	30 12	3084	3426	6510	52 63	570	4	574	0 7

Indian " Immigrant " Group (No ages available)

Married	4559
Unmarried	84
Total	4643
% Unmarried	1 81

collected from the records of the Registrar of Births and Deaths for European, Coloured and Bantu births, and from the records of the Protector of Indian Immigrants for " Passenger Indians " and " Indian Immigrants." Every live birth, multiple and single, for the year 1948 was extracted from the records. Since Indian birth registrations are often very long delayed, sometimes until school-going age, the 1948 records were used rather than more recent data, in order to obtain information on babies born in 1948, but registered later. Although registration of birth is compulsory by law for all racial groups, the only group fully covered by registration is the European. Registration is particularly incomplete among the Bantu where most of the births registered are of babies born in the maternity hospitals.

It will also be noted that there are two distinct Indian communities recorded. The first, the " Indian Immigrant " group are the descendants of the Indians who were brought from India from 1860 onwards by the Government of Natal to work in the sugar-fields, or as domestic and general labourers. The " Passenger Indians " are non-indentured Indians who paid their own passage fare from India to this country, and settled in Natal, mainly as traders among the indentured Indian population (FERGUSON-DAVIE, 1951). The Passenger Indians represent a small percentage of the total Indian population of Natal, an approximate estimate being 10 per cent., and they are predominantly Moslem. Most of the Indian trade is in their hands, and they are better off financially than the Indian Immigrants who are mainly Hindu, and predominantly economically depressed unskilled labourers. Birth and death records for these groups are kept separately. Unfortunately the ages of the Indian Immigrant mothers at the time of birth of their babies is not recorded in the registers. For all the other groups the age is given.

RESULTS AND DISCUSSION.

Table I compares the European, Coloured, Bantu and Passenger Indian percentage of illegitimate births by age of mother. Only the total for Indian Immigrants is shown. The European, Coloured and Bantu births show a common feature in that most of the illegitimate births are of young mothers. The number of illegitimate births of Passenger Indians is so small that a very much greater sample would have to be used to see if the same trend is present there as well. There is a striking contrast, however, in the percentage of legitimate and illegitimate births in these groups. The Passenger Indians have the highest percentage of maried mothers, 99.3 per cent. They are closely followed by the Europeans with 98.38 per cent. married, which figure hardly differs from that of the Indian Immigrant mothers, 98.19 per cent. The Coloureds, however, have only 69.88 per cent. of their mothers married, and the Bantu have more unmarried than married mothers, 47.37 per cent. being married.

However inaccurate the registration figures may be, they are startling enough to warrant an exploration of the sociological background of these racial groups, in order to measure the effects illegitimacy may have on their respective communities.

Among Europeans strong social disapproval is shown towards unmarried mothers and their offspring. It is the exception for an unmarried girl to keep her baby. When the records of two large European maternity hospitals in Durban were examined it was found that in almost all cases European illegitimate babies are adopted, and are weaned during their stay in the hospital preparatory to that adoption (SALBER, 1955). The sanctions of European society would tend to keep the incidence of illegitimacy low, and both unmarried mothers and their babies would suffer.

The Indian Hindu community is very strict in its attitude to premarital conception. The family is a large well-knit unit and the girls are closely chaperoned. They maintain their traditional marriage customs. The Hindu in South Africa are, however, in a transition period. The traditional joint family is gradually breaking down, owing to unsatisfactory conditions of housing, increasing education of girls, and their gradual employment outside the home in factories and domestic work. This results also in a conflict between the generations. Caste regulates marriage and especially among upper-caste families violation of regulations involves out-casting. Marriage is a family affair and there is no divorce among the Hindu. The family regard illegitimate conception as a disgrace, and the mother, though not the child, is stigmatised. Hindu girls who become pregnant before marriage have been known to commit suicide rather than bear the disgrace. Full marriage rites cannot be performed for an unmarried mother, though she may have the opportunity to marry an old man or a widower.

In a preliminary field study of illegitimacy in Merebank Indians, KUPER (1953) found that in a number of cases the girl's parents shifted from the area to avoid the disgrace. Every attempt was made by them to arrange for the girl's marriage to the father of her child, although no full ceremony could be performed since this would involve the marriage of the unborn child as well. If a marriage did not take place, they tried to have the baby adopted. The boy's parents were usually very unwilling to accept the girl. In only two of the 22 cases studied did the boy marry the girl ; the other girls remained unmarried and two of them became pregnant again by other men. In fourteen cases the baby remained with the mother and her parents, in four cases the babies were adopted by childless relatives of the mother.

The low incidence of illegitimacy among the Indian group is therefore not surprising, but it is possible that the true figure may be a little higher than is actually recorded since illegitimate births may be concealed by non-registration, late registration, or registration after adoption.

I know very little about the Moslem community but it appears that the girls are even more strictly kept than among Hindus. They are hardly allowed to venture outside the family fold, and they have even less schooling than the Hindu girls. So strong is the family solidarity and so carefully are the girls looked after that Indian health assistants working at the Institute of Family and Community Health expressed surprise that any illegitimacy at all was found in this community. It is interesting in this regard, that the few cases which did occur, were among older rather than younger women, but the number is too small to enable one to decide whether this is a chance occurrence or not.

For the purpose of official statistics, the term Coloured " embraces not only the Cape Coloured and 'other persons of mixed race,' but also the Cape Malays, the Bushmen, and the Hottentots. . . In 1936, not less than 75.21 per cent. of all Coloured were classified as ' Cape Coloured." (SONNABEND, 1949).

The attitude of the Coloured folk in Durban to illegitimacy varies depending on whether the parents come from the country or are townspeople. Those coming from the country are much stricter and deplore their daughters' " bad ways." In the town, however, illegitimacy is perforce accepted now, though with shame. There is no stigma attached to the baby, and the unmarried mother very often marries subsequently. Studies of this community at the Institute of Family and Community Health, showed that they lacked a cohesive family or community life, and a unifying tradition.

The Bantu present a rather different problem. Here we have a change of attitude which is very marked and very rapid, and which is an important aspect of the tremendou revolution in the habits of the Bantu since their contact with Europeans.

Customary marriage is legalised by the transfer to the wife's people of *lobola* (Nguni or *boxadi* (Sotho), a material consideration generally taking the form of cattle (SHAPERA 1934). The primary function of *lobola* is to legitimise the marriage and its resultant offsprin All children born to a woman for whom *lobola* has been transferred or promised ar considered to be the legal offspring of her husband, even though he may not be thei physiological father. Children born to a woman for whom *lobola* has not been transferre or contracted are regarded as illegitimate. They belong to their mother's family an kin, their father having no claim to them unless he makes a special payment.

A child born of an adulterous intercourse does not belong to its natural father, bu to its sociological father. The child born to a widow at her late husband's home is regarde as his, it bears his name and has the same rights as the children born during her husband' lifetime, particularly when the widow has been taken over by her husband's brother c some other approved relative under the levirate custom (KRIGE, 1937).

The *lobola* system has survived although the missionaries strenuously opposed i It has, however, changed in some respects, becoming more of a commercial transactio in many cases money being substituted for cattle.

According to SHAPERA (1937), there has also been a marked change in the relationsh between parents and children. The decline of ancestor worship has deprived the fath of his rôle of family priest, and the abolition or modification of the old initiation cer monies has led to a slackening of family discipline. Labour migration deprives the fami of parental authority for long periods at a time, and the sons migrate to the towns ar live independently of the family. The young people no longer accept the guidance their parents in all things, but tend to do as they please. Sexual life in the Reserves h been affected. The decline of polygamy means that many women can no longer mar young. When young men leave the Reserves, it leads to a disproportion of the sexe and as a result the age of marriage rises. Sexual morality has consequently relaxe particularly since the young are now much more independent than of old, and illegitima is becoming increasingly common in the Reserves, although it is still frowned upon l parents and elders.

Migration takes place for various reasons, but the most important reason is econom The peculiar feature of Bantu migrant labour is that so many workers are regarded and regard themselves as merely temporary residents in the town. They work in t towns, going back periodically to their homes in the Reserves. There is a growing te dency, however, for the family to establish itself in the town, but this is restricted by la of land and housing. The migratory labour system has far-reaching consequences, a is disrupting the stability of family life as it was in the Reserves. (VAN DER HORST, 194

" Bantu urbanisation has not been a straightforward process of the townward mig tion of a rural population..." A permanent labour force in secondary industry depen dent on a cash wage and living a family life in the town is gradually developing but the is also a large floating population of whom the great majority are men. The ratio Bantu men to women in the towns is often two to one, rising to four to one in certa places. The presence of large numbers of unattached males leads inevitably to casu unions and an increase of prostitution. There are no forces to integrate the developi urban society, for the sanctions of the tribe no longer operate (HELLMANN, 1949). Unc these conditions illegitimacy becomes extremely common as is reflected in the figures of this report. The parents are very worried about this, but are powerless to prevent it.

It is impossible to say whether the actual incidence of illegitimacy among Durban Bantu would be higher or lower if registration were complete. Births outside of the hospitals are more likely to be notified by married people, but the great bulk of registrations are from hospitals, whose figures are probably not weighted in one or the other direction.

A very important factor, however, which would tend to exaggerate the incidence of illegitimacy, is that, although the registration clerks accept customary as well as civil marriages, they do not know the family background of the people concerned, and many cases which may be recorded as illegitimate may in fact be sociologically legitimate in the Bantu community.

It was decided therefore to investigate the incidence of illegitimacy in two communities served by the Institute of Family and Community Health, and use was made of the birth records of Bantu babies born in Lamont Location, Durban, from 1950 to 1953, and of Indian babies born in the Springfield Housing Scheme, from 1948 to 1952. (Table II).

TABLE II. Percentage of illegitimate births according to rank of child, in two communities served by the Institute of Family and Community Health.

	Bantu : Lamont 1950-53			Indian : Springfield 1948-52		
	All births	Primip.	Multip.	All births.	Primip.	Multip.
No. of total births*	977	193	750	415	55	329
% Legitimate	68.4	35.8	77.2	96.1	83.6	98.2
% Illegitimate	28.4	61.1	19.7	3.9	16.4	1.8
% Unmarried but stable union	3.2	3.1	3.1	—	—	—

* It must be noted that the numbers of primiparae and multiparae do not add up to the numbers of total births, as the rank of the child was not known in many cases.

It will be seen that there is far less illegitimacy in Lamont than in Durban as a whole, 28.4 per cent. as against 52.63 per cent. One would expect this result since Lamont Location is a family housing scheme. It has the disadvantage, however, of having a barracks for single men on its outskirts. The young girls again have most of the illegitimate births, only 35.8 per cent. are married and 61.1 per cent. unmarried when they have their first babies.

The other interesting feature of Lamont is the presence of a group of people who are not married, either by civil or customary rites, and yet have stable unions, so that the child is born into a stable family and to all intents and purposes is not sociologically illegitimate. Such children would certainly be reflected as illegitimate in the figures collected by the Registrar of Births and Deaths.

The Springfield Indian figures (mainly Hindu) on the other hand show an increase in the percentage of unmarried mothers, 3.9 per cent. as against 1.81 per cent. for Durban.

This is probably due to the fact that at the Springfield Health Centre we knew about all the births, and illegitimacy would not be concealed as it might be in Durban as a whole by non-registration, or late registration by adoptive parents. The young mothers, again, are responsible for most of the illegitimate births, 16.4 per cent. of the primiparae being unmarried.

On the whole medical practitioners are interested in illegitimacy chiefly from the point of view of infant morbidity and mortality. It is well known that in European society illegitimate infants have a higher infant mortality rate than legitimate infants, the figures given in the Maternity in Great Britain Report (1948) being 65 per thousand live births for illegitimate as compared with 45 for legitimate births.

The infant mortality rates for Durban over the period 1947 - 1951 (calculated from Annual Reports of the Medical Officer of Health) were found to be : European 28.4, Coloured 85.3, Bantu 346.4, and Asiatic 82.2. The difference between the Bantu and Indian rates is striking, the more so as the Indian babies weigh so much less at birth and grow so much more slowly than do Bantu babies (SALBER, 1955).

On the other hand PATON and FINDLAY (1926) stressed the importance of maternal efficiency in the nutrition and health of children. They quoted ASHBY (1915) to the effect that, in efforts made in New York, to reduce mortality, it was the unanimous opinion of the doctors concerned that neither the surroundings of the infant, nor the exact character of the milk consumed were as important factors in the health of the baby as the intelligent care of the mother. It seems reasonable to use figures of incidence of illegitimacy as a measure of family stability and to assume that where the figures are high maternal efficiency is likely to be low and infant mortality rates high.

The evidence presented in this paper strongly suggests that Indian urban family life is more stable than that of the Bantu. The unmarried Bantu mother (particularly the young girl) is hardly likely to be efficient in the rearing of her offspring. Since *more than half* the Bantu babies registered in Durban in 1948 belonged to unmarried mothers, it is hardly surprising that the Bantu infant mortality rate is so high.

The Indian mother on the other hand is seldom unmarried, and lives in a community with very strong family ties. Despite the poverty and poor nutritional state of the Indians, their babies live. I feel that in these two communities, at least, there is a very strong positive correlation between incidence of illegitimacy and infant mortality rates.

SUMMARY.

(1) Illegitimacy is defined in relation to the society in which it occurs.

(2) The incidence of illegitimacy is given for the four racial groups in Durban in 1948. The incidence is lowest of all in the " Passenger " Indians and highest in the Bantu.

(3) Illegitimacy is inversely related to age of mother.

(4) Some sociological data are given for the Coloured, Bantu and Indian groups, and the attitude to illegitimacy in the four races is discussed.

(5) It is concluded that incidence of illegitimacy is a measure of family stability, and indirectly of maternal efficiency, and that there is a strong positive correlation between incidence of illegitimacy and infant mortality rates.

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FURTHER OBSERVATIONS ON THE LIVER, PANCREAS AND KIDNEY IN MALNOURISHED INFANTS AND CHILDREN

II. The Gross Composition of the Liver.

by

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The fatty liver of kwashiorkor still presents a number of unsolved problems :

(i) Is it a specific feature of the kwashiorkor syndrome, differentiating it from marasmus and other forms of malnutrition ?

(ii) Does it result, as has often been suggested (Waterlow, 1948 ; Trowell, Davies and Dean, 1954) from a calorie intake which is relatively high in relation to that of other nutrients ?

(iii) Does the deposition of excess fat in the liver go hand in hand with a loss of cytoplasmic protein (Waterlow, 1955) ?

(iv) Is the degree of fatty infiltration related to the general condition of the patient ? Can it be regarded as an indication of the severity of the malnutrition ?

A certain amount of information on these points, particularly the last two, has been obtained by biopsy studies. In the past few years we have made measurements of the fat content in biopsy specimens of the liver from over 100 malnourished infants and young children (unpublished observations). The most extreme fatty infiltration (fat = 50 per cent. or more of the wet weight) has only been found in fatal cases. Apart from this, no consistent relationship has been observed between the fat content and the general condition of the patient, the course of the disease, or the response to treatment.

In a small series of cases with fatty livers measurements have also been made of protein content in relation to nuclear nucleic acid (DNA) before and after treatment (Waterlow and Weisz, 1956). On this basis it was found that the liver before treatment had lost on the average some 40 per cent. of its cytoplasmic protein. The cases, however, were too few for any relation to be established between the amount of fat and the degree of protein depletion. Moreover, this type of investigation has serious limitations, both of technique and of interpretation.

For this reason it seemed useful to reinvestigate the problem by an analysis of post-mortem material. Since the weight of the liver is known, it is possible to calculate total liver protein and fat in absolute terms, and the figures can be compared with those of a normal or ideal standard. Such a standard is arbitrary, but at least it provides a fixed basis of comparison.

The main aim of the present work has therefore been to see whether, in a group of malnourished infants who died, any relation could be found between the following variables : (a) growth, as assessed by height and weight in relation to age; (b) degree of fatty infiltration of the liver ; (c) oedema ; (d) degree of protein depletion of the liver.

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* We are indebted to Dr. D. B. Jelliffe and Dr. E. Back for allowing us to include in this paper material from cases under their care.

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R OBSERVATIONS ON THE LIVER, PANCREAS AND KIDNEY IN MALNOURISHED INFANTS AND CHILDREN

II. THE GROSS COMPOSITION OF THE LIVER.

by

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atty liver of kwashiorkor still presents a number of unsolved problems :

(i) Is it a specific feature of the kwashiorkor syndrome, differentiating it from marasmus and other forms of malnutrition ?
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Having established certain relationships, we then try to see how these fit in with the clinical diagnoses made before death, and with the general concept of two distinct syndromes — " kwashiorkor " and " marasmus."

Chemical Methods.

Analyses were made on tissue which had been fixed and stored in neutral buffered formalin, sometimes for periods of 2 years or more. There is clearly opportunity here for artefact. However, it was found that organs kept in formalin showed no significant change in weight compared with the fresh state. Water content was measured by drying at 100° C. The dry tissue was then extracted overnight with hot ethyl ether in a Soxhet apparatus, and briefly dried again in the oven. The fat content was calculated from the difference in weight. This simple method of fat extraction is not completely accurate : it leaves behind lipids — probably phospholipids — amounting to about 3% of the fresh weight of the tissue. It is, however, sufficiently accurate for the present purpose ; in effect, the fat extracted represents excess fat. Nitrogen in the dry residue was measured by micro-kjeldahl. Protein was calculated as N x 6.25 : this gives a slight overestimate, since no allowance has been made for non-protein N. These analyses were made on 200 - 400 mg. of tissue (fresh weight), since usually only small pieces of liver were available. There is a certain sampling error, since in some cases it is obvious, both to the naked eye and microscopically, that fatty infiltration is not absolutely uniform The results must therefore be regarded as estimates rather than exact statements.

Standards.

We have used as standards the figures given by HOLT and McINTOSH (1941) for body weight, and by COPPOLETTA and WOLBACH (1933) for height and liver weight. The total protein content of the normal liver has been taken as 17% of the liver weight. In our series the heights, weights, and total liver protein have been calculated as percentages of the expected or so-called normal values at the appropriate age. These normal values have been obtained from American, not West Indian, children, and represent averages with a large scatter ; they may therefore rightly be called artificial. However, in the present paper we are not concerned with what is normal or abnormal. The standards have simply been used as a convenient method of weighting the results for age, so that comparisons can be made between groups and within groups. They are referred to throughout as the *expected* values (for height, weight, liver protein, etc.).

Selection and classification of cases.

Liver tissue was available for analysis from 51 babies dying between the ages of 2 months and 3 years. These form part of the series reported in a previous paper (BRAS *et al*, 1956). The cases have been divided into 2 groups — those dying primarily from malnutrition, and those dying from infections and miscellaneous diseases (control group). This group was made up as follows : acute infections 13 : disseminated tuberculosis 4 : sickle-cell anaemia 1 : heart-block 1 : veno-occlusive disease of the liver 1 ; total 20 cases.

In an earlier paper (BRAS *et al*, 1956) mention was made of the difficulty that sometimes arises in deciding whether a case should be assigned to the malnourished or to the control group. This difficulty is only to be expected, since terminal infection is usual in babies dying of malnutrition, and conversely, an infant with a severe infection rapidly becomes malnourished. The criteria we have used are the clinical diagnosis at the time of admission, the pathological diagnosis of the cause of death (infection, etc.) and, in doubtful cases, the degree of deficit in weight and height. It should be emphasized that we have tried not to use the condition of the liver as a criterion, and not to classify a case as malnourished simply because a fatty liver was found at autopsy. To do this would be to introduce a bias which would be fatal to the aim of the investigation.

In order that the malnourished cases can be compared with those previously reported from Jamaica and other parts of the world, we have divided them into 3 sub-groups : (A) kwashiorkor (16 cases) ; (B) marasmus (9 cases) ; (C) cases in which malnutrition and infection seemed to be factors of roughly equal importance (6 cases).

The main criteria for the diagnosis of kwashiorkor were oedema and enlargement of the liver. In 9 of the 16 cases there was dyspigmentation of the hair, in 9 also some degree of dermatosis, and in 7 lesions of mucosae. The marasmics showed no specific signs, other than dehydration and weight loss, except for one infant with dermatosis and mucosal lesions. Oedema was present in 4 of the 6 cases complicated by infection.

Again, it is difficult to decide, in the border-line case, whether or not the diagnosis of kwashiorkor is justified. Different observers might group the cases in slightly different ways, according to the emphasis they placed on the various signs. But this does not affect the main object of this paper, which is to see what correlations can be established between liver fat, body weight, etc., within the malnourished group as a whole.

RESULTS

The findings in the various groups are shown in Table I. The clinical characteristics of kwashiorkor and marasmus, as they are seen in Jamaica, have been described in previous papers (Waterlow, 1948 ; Jelliffe, Bras and Stuart, 1954). Therefore only 2 points will be considered in more detail — oedema and hepatomegaly.

Oedema. Since the oedema of kwashiorkor is usually accompanied by hypoproteinaemia, it is tempting to regard it as evidence of protein depletion. However, it has often been pointed out (Trowell, Davies and Dean, 1954) that even in kwashiorkor this relation is not invariable. Many workers have reported serum protein levels of more than 5.0 g. per 100 ml. in the presence of oedema. In this series the opposite has also been found : in 3 marasmics the serum total protein was 5.0 g. per 100 ml. or less without any clinically detectable oedema. Only 4 measurements of serum protein concentration were made in the marasmic group, but the mean of these differed very little from the mean in the kwashiorkor group :

Kwashiorkor : 11 cases of which 9 with oedema : mean total protein 4.7 g. per 100 ml.
Marasmus : 4 cases, of which none oedematous : mean total protein 4.9 g. per 100 ml.

Another point of interest is the common coexistence of oedema of the feet with signs of dehydration, such as sunken eyeballs and fontanelle, and inelasticity of the skin of the trunk. This combination was present in 6 of the cases of kwashiorkor, and in 4 of the group with infection. Perhaps the distribution of oedema in some parts of the body and of dehydration in others is determined by local differences in circulatory dynamics. This is further evidence that the serum protein level cannot be the only factor determining the retention of oedema fluid. Other possible factors that have been put forward are a decreased destruction of antidiuretic hormone (Gopalan, 1955) and a retention of sodium secondary to potassium loss (Hansen and Brock, 1954).

Clinically, we look upon oedema as one of the diagnostic features that distinguish kwashiorkor from marasmus. Bio-chemically, on the basis of serum protein levels, the distinction does not seem to be clear-cut. It must be recognized that, as long as we do not know the cause of the oedema, to use it as a diagnostic criterion is purely empirical.

Height and body weight. Table I. shows that the loss of body weight was greater in the marasmic group (B) than in kwashiorkor (A). The difference is statistically just significant (P = 0.05), but one cannot conclude that there is a real difference in tissue mass, since the cases of kwashiorkor were oedematous*, whereas the marasmic babies were dehydrated. Moreover, it is well recognized that in kwashiorkor the subcutaneous fat is relatively well preserved. Some of the cases in this group were of the type that has aptly been described by JELLIFFE *et al.* (1954) as " blubbery." Therefore it is not impossible that the actual cell mass may even be less in kwashiorkor than in marasmus. Without analysis of the whole body it is difficult to substantiate this point.

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* The body weights recorded were in most cases those measured at autopsy. Oedema was frequently still present.

TABLE I.

	MALNUTRITION.				CONTROL.
	A. Kwashiorkor.	B. Marasmus.	C. Malnutrition with infection.	Total malnutrition.	D.
Number of cases	16	9	6	31	20
Sex : male/female	*0.8*	*2.0*	*1.0*	*1.1*	2.1
Age, months : mean	10.5	9.0	10.5	10.3	10.75
range	4–22	4–17	7–17		2–36
Number with oedema	14	0	4	18	3
„ „ dehydration	6	6	6	18	6
„ „ hepatomegaly*	11	3	2	16	7
„ „ fatty liver†	15	3	3	21	9
Body weight, as % of expected wt.‡ : mean	58	47	57.5	54.8	79.1
range	32–79	33–65	39–78		43–107
Height, as % of expected ht‡ : *mean*	94	*89*	93	92.3	99.6
range	76–106	82–98	89–100		84–116
Liver wt., as % of expected wt‡ : mean	153	69	99	118	113
range	84–377	40–116	55–141		43–300
Total excess liver fat, grams : mean	145	38	57	97	53
range	0–325	0–200	0–131		0–296
Total liver protein, as % of expected protein mean	67	51.5	64	61.5	80.3
range	35–110	40–67	43–90		42–118
Liver water/protein mean	7.1	5.4	5.7	6.34	5.51
range	4.3–9.4	3.4–7.2	3.4–8.0		4.3–8.3

* liver edge 1½ fingers' breadth or more below costal margin.
† fat concentration more than 15% of wet weight.
‡ as per cent of the weight, height, and liver weight for a normal child of the same age.
Figures for body weight from HOLT and MCINTOSH (1941).
Figures for height and liver weight from COPPOLETTA and WOLBACH (1933).

The difference in height between the sub-groups A and B is not significant. However, the difference between the malnourished cases as a whole and the control group is significant ($P < 1\%$). It is noteworthy that the average height in the control group was normal. For the purpose of assessing the degree of malnutrition the height is perhaps more useful than the body weight, because it is affected by fewer variables. Naturally, single figures have no meaning, but the group averages show that in the malnourished cases there was an undoubted growth failure, which was probably more severe and more long-standing in the marasmics than in the others.

Hepatomegaly and liver weight. It has been observed previously that hepatomegaly is a very prominent feature of kwashiorkor in Jamaica (WATERLOW, 1955). Since the assessment of enlargement of the liver is subject to a great deal of observer error, some workers have questioned the significance of this finding. In the present series hepatomegaly, defined as a liver edge palpable 1½ fingers' breadth or more below the costal margin, was found in 23 out of 45 cases of all groups in which a record was made. These clinical impressions can be compared with the absolute weights of the livers found at autopsy. For this purpose there is a choice of two standards : (a) the liver weight may be related to the expected liver weight in a normal child of the same age ; (b) the liver weight may be expressed as a percentage of the actual body weight. The results by both methods of comparison are shown in Table II.

TABLE II. Comparison of hepatomegaly and liver weight.

		Cases with hepatomegaly.	Cases without hepatomegaly.
No. of cases		23	22
(a) Liver weight as per cent. of " expected " liver weight. at same age.	mean	141	89
	range	50 - 377	40 - 141
(b) Liver weight as per cent. of body weight.	mean :	6.2	4.35
	range :	(3.2-16.0)	(1.0-7.1)

Comparison (a) shows that in the cases with hepatomegaly the livers were substantially larger than in normal children of the same age. When body weight is taken into account (comparison (b), the increase in size is even more striking, as is to be expected, because of the low body weights. The normal ratio of liver weight to body weight in this age group is 2.9 per cent. In the cases with hepatomegaly this ratio is more than doubled. In one infant there was an enormous liver, amounting to nearly one sixth of the body weight. Even in the cases without clinical hepatomegaly the liver weight on the average amounted to 4.35 per cent. of the body weight, showing that the liver was less reduced in size than the rest of the body.

The increase in size is caused by fatty infiltration. Of 23 cases with hepatomegaly, 17 had moderate or severe fatty change (fat content more than 15 per cent. of the wet weight). One case need not be considered further, since there was heart-block and severe anaemia, which may have been associated with heart failure. In 5 cases hepatomegaly was recorded, but the livers contained no excess of fat. All these babies were, however, very severely malnourished, so that the livers, although absolutely small, were still large in relation to the actual body weight.

Of the 22 cases in whom enlargement of the liver was not observed clinically, 7 had severe fatty infiltration. In 3 of these the liver was appreciably increased in size (average weight = 130 per cent. of expected weight). In the other 4 the livers, although very fatty, were not enlarged. This is presumably because the accumulation of far was counterbalanced by a decrease in water and protein — a point that will be considered in more detail later.

It may be concluded that the clinical impression of hepatomegaly is not only correct more often than not, but in fact underestimates the incidence of liver enlargement in these cases, whether measured in absolute or in relative terms. In the absence of ascites and other evidence of veno-occlusive disease (BRAS, JELLIFFE and STUART, 1954) enlargement of the liver in this age-group is presumptive evidence of fatty infiltration. Cases of extreme marasmus may, however, prove an exception to this rule.

Liver Fat. A number of points must be considered under this heading :

(i) *Method of expression.* It is usual to express liver fat as a percentage of the wet weight or dry weight. This, however, is misleading, since it involves a ratio of the form $\frac{F}{F + K}$, where F = amount of fat, and K = amount of substances other than fat. As F grows larger, the ratio of $F/F + K$ increases, but at a diminishing rate. This is illustrated by the following figures from our series :

TABLE III. Liver fat expressed as per cent. of wet weight and as total fat.

Fat content. % of wet weight.	No. of cases.	Average total liver fat, gm.
6 - 15	5	19
16 - 25	8	45
26 - 35	8	131
36 - 45	8	137
46 - 55	6	239

The point to be emphasized is that if a liver containing 50% of fat is compared with one containing 10%, the total fat increases more than 10 times, whereas the concentration increases only 5 times. Thus with very fatty livers the usual method of expression underestimates the severity of the fatty infiltration. This is one reason why, with very fatty livers, the histological grading may be misleading, as was pointed out in the preceding paper (BRAS *et al*, 1956). When the liver weight is not known, as with biopsy specimens, the difficulty can be avoided by relating the liver fat to the non-fat solids, instead of to the wet weight or the dry weight.

(ii) *Incidence of fatty liver in different clinical groups.* Table I. shows that fatty livers are most frequent and most severe in the kwashiorkor group. However, an element of selection may be involved here, because, as has been shown, fatty liver is usually associated with hepatomegaly, and this was one of the criteria used in the clinical classification of the cases.

Fatty livers also occur sporadically in all the other groups — in the marasmics there were 2 severely fatty and 1 moderately fatty liver ; of the malnourished cases complicated by infection, 3 out of 6 had fatty livers, all severe ; in the control group 6 livers were very fatty and 2 moderately fatty. 3 of the 4 children dying of tuberculosis had fatty livers.

In one sense these findings merely repeat the difficulty discussed in the introduction, of making any hard and fast clinical classification. However, the problem cannot be disposed of simply by saying that some of the cases were wrongly classified. It is well known that in temperate countries also fatty livers are sometimes found in infants dying of infections, such as gastroenteritis, and particularly in tuberculosis (GIRARD, PLAUCHU and LOISY, 1954). The question therefore arises : is the fatty liver of infection something different in nature and cause from that of malnutrition ? Alternatively, is it simply the result of secondary malnutrition or of an extra stress imposed on a previously malnourished body ? The second explanation seems probable in our cases in group C, and perhaps in the others also. However, no definite answer can be given without further information about the frequency and severity of fatty liver in infants dying of infection, in countries where primary malnutrition may be ruled out.

(iii) *Correlations with other measurements.* Instead of attempting to establish differences between the various somewhat arbitrary clinical groups, it is more profitable to determine what associations can be established between the various features within the malnourished group as a whole.

(a) In the whole series (malnourished + controls) there is a significant association ($\chi^2 = 4.5$; $P = 5\%$) between oedema and a severely fatty liver (fat content more than 50 gms. : fat concentration more than 20 per cent.). Fatty liver is in fact more common than oedema ; exceptions to the association are not infrequent, and fatty liver is more often found without oedema than the opposite. This confirms the impression formed in an earlier study in the West Indies (WATERLOW, 1948), that oedema, which is often the cause of the child being brought to hospital, is a late event, whereas fatty liver may be of relatively long standing. It is noteworthy that in the kwashiorkor group there was usually a rather long history, averaging 7.7 weeks, of vomiting and difficulty in feeding ; perhaps the fatty liver was developing during this time.

(b) In the malnourished cases (sub-groups A + B + C) there is a significant correlation between the amount of liver fat and both body height and body weight.

(for height $r = +0.58$. $P = 0.1\%$.
(for weight $r = +0.53$. $P = < 1\% > 0.1\%$.)

In other words, fatty livers are less common and less severe in infants who show the most severe growth failure.

(c) In the malnourished group as a whole there is a correlation which is barely significant between the amount of liver protein and the amount of liver fat ($r = +0.34$; $P = 5\%$). This means that in the liver of a malnourished subject the two pathological processes — increase in fat and decrease in protein — tend to vary in opposite directions in magnitude. This conclusion was unexpected ; it had been thought that fatty infiltration and loss of protein might be changes that went on hand in hand, perhaps with a common cause (WATERLOW, 1955).

Liver protein and water content. In the whole series the total liver protein is reduced roughly *pari passu* with the body weight. The reduction is greater in the marasmic group than in the cases classified as kwashiorkor ($P = 5\%$). Therefore, judging by the findings in the liver, we cannot say that kwashiorkor is specifically a state of protein depletion since marasmic cases are even more depleted.

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(c) In the malnourished group as a whole there is a correlation which is barely significant between the amount of liver protein and the amount of liver fat ($r = +0.34$; $P = 5\%$). This means that in the liver of a malnourished subject the two pathological processes — increase in fat and decrease in protein — tend to vary in opposite directions in magnitude. This conclusion was unexpected ; it had been thought that fatty infiltration and loss of protein might be changes that went on hand in hand, perhaps with a common cause (WATERLOW, 1955).

Liver protein and water content. In the whole series the total liver protein is reduced roughly *pari passu* with the body weight. The reduction is greater in the marasmic group than in the cases classified as kwashiorkor ($P = 5\%$). Therefore, judging by the findings in the liver, we cannot say that kwashiorkor is specifically a state of protein depletion since marasmic cases are even more depleted.

In the cases of kwashiorkor, there is a significant increase in the water content of the liver. The mean ratio of water to protein was 7.1 in the kwashiorkor group, compared with 5.5 in the controls. The difference is significant at the level of 1%. This increase in water, it may be supposed, is related to the presence of oedema ; yet it seems doubtful if all the additional water can be extracellular. The water content of the liver in these cases is on the average some 25 per cent. higher than in all the other groups. HARRISON (1953) found that in the normal rat liver the extracellular water amounts to about 20 per cent of the total water. Applying this figure to our cases, if all the excess water were in the extracellular phase, the volume of that phase would be more than doubled. Anatomically there does not seem to be much space in the liver for the accumulation of such a large amount of extracellular fluid, particularly when the liver is distended with fat, and microscopically no evidence of oedema has been noted. The possibility therefore remains that the excess fluid is intracellular. Too much stress should not be put on this, since the analysis of tissues after prolonged fixation in formalin clearly opens the way to many artefacts ; however, the possibility is being investigated.

DISCUSSION

Three main points emerge from this investigation : the relationship of fatty liver to body weight and height, to total liver protein, and to oedema.

(1) The first relationship, that the cases with fatty liver show the least growth failure, may be interpreted in two ways :

(a) *Fatty infiltration of the liver cannot develop unless the nutritional conditions are such as to allow* at least some degree of growth. This has been well established in the rat by the work of MULFORD and GRIFFITH (1942), BEVERIDGE, LUCAS and O'GRADY (1945), and HANDLER (1944). In fact, growth seems to potentiate the development of fatty liver by competing for essential metabolites. The fact that the cause of the fatty liver may not be exactly the same in man as in the rat does not mean that the same general condition cannot hold. There are many other phenomena of the same kind. The best-known example is the relationship of carbohydrate intake to beri-beri. Another example is the fact that rickets and kwashiorkor seldom occur together, even in populations where both diseases are found (VERGARA and WATERLOW, 1956). Presumably this is because in kwashiorkor the rate of growth is too low to allow the signs of rickets to develop — in other words, for vitamin D to become a limiting factor.

This explanation of the correlation between liver fat and growth fits in with the idea that fatty liver results from an unbalanced diet in which calories are relatively less deficient than other nutrients. In kwashiorkor the limiting factor is protein, whereas in marasmus it is calories. That hypothesis was put forward in an earlier study (WATERLOW, 1948), and is a central part of the explanation of the kwashiorkor syndrome developed by TROWELL and his colleagues in Uganda (TROWELL, DAVIES and DEAN, 1954).

(b) *The second possible explanation is that fatty liver, like infection, is harmful* and increases the chances of death, If this is so, an infant with a fatty liver might tend to die at an earlier stage in the development of general malnutrition and growth failure than one without. However, as was stated in the introduction, clinical and biopsy studies over the last few years have suggested that fatty infiltration is not particularly harmful, except in the most extreme cases (fat content more than 50 per cent.). To prove the point it would be necessary to compare the course of cases which were in all respects identical, except for the degree of fatty change, and this is very difficult.

(2) The fact that fatty livers tend to be less depleted of protein is of considerable interest. It means that the two abnormal processes occurring in these livers — increase in fat and decrease in protein — are disengaged. Presumably, therefore, although they often occur together, there cannot be any direct causal connection between them.

The figures also show that we cannot define kwashiorkor as simply a state of protein depletion, since marasmics are even more depleted — at least as far as the liver is concerned, and probably in the body as a whole. The *degree* of protein depletion does not provide a basis for distinction between the two conditions.

(3) The statistical association of oedema and fatty liver adds substance to the concept of kwashiorkor as a distinct entity. In a sense this merely corroborates the impressions of many clinicians. At the Jamaica Conference (WATERLOW, 1955) it was pointed out that progress can best be made by an analysis of associations. Almost any association can be found if it is looked for — that is to say, if the element of selection is not excluded. This has happened in many accounts of kwashiorkor, in which nothing is said about the cases of malnutrition which are *not* diagnosed as kwashiorkor. The question always is : is the association real or fortuitous ? The present very limited series suggests that in Jamaica, at least, the association is real.

Oedema and hepatomegaly (which, as has been seen above, is presumptive evidence of a fatty liver) might be taken as *the* diagnostic criteria of kwashiorkor in Jamaica. Dyspigmentation of the hair and changes in skin and mucosae tend to be associated with these two, but the numbers are too few for statistical test. There will always be individual cases which are difficult to classify ; but this need not weaken the concept of kwashiorkor as a definite syndrome, the result of a process which in some way differs from the process leading to marasmus.

What, then is the difference between the two processes ?

As has been argued, one element in the difference may be the calorie intake. It is not difficult to understand a relation between calorie intake and the development of a fatty liver. It is harder to see a connection between calorie intake and oedema — the other cardinal feature of kwashiorkor — since the post-war work on famine oedema in adults suggests that this develops only when the calorie intake is very low (MCCANCE, 1951). In these adults, however, there is no fatty liver and no histological evidence of liver damage (UHLINGER, 1948 ; SHERLOCK, 1951). The work of GOPALAN (1955) suggests that in kwashiorkor oedema might be secondary to liver damage, through failure to inactivate the antidiuretic factor.

In both marasmus and kwashiorkor there is depletion of body protein. We have found no evidence that the two can be distinguished by the degree of protein depletion. However, it has been pointed out that states of protein depletion may differ not only in degree but also in pattern (WATERLOW, 1955). This might be the basis of the difference between the two syndromes. TROWELL (1953) has advanced the hypothesis that " the marasmic lives on its own meat." In less picturesque terms this might be restated as follows : the breakdown of protein, mainly from muscle, to provide calories produces a metabolic pattern which in some way protects the organs with a high protein turnover, such as liver and pancreas, in spite of the greater net loss of nitrogen from the body. Experiments are in progress to test this hypothesis.

SUMMARY

(1) Measurements have been made of the fat and nitrogen content of the liver in 31 infants less than 3 years old dying of malnutrition, and in 20 control infants of the same age-group dying of infections and other diseases. The malnourished group contains 16 cases diagnosed as kwashiorkor, 9 cases diagnosed as marasmus, and 6 cases of severe malnutrition complicated by infection.

(2) In the malnourished group enlargement of the liver was often noted on clinical examination. This impression was confirmed at autopsy : the liver weights were much higher than normal, whether expressed in relation to age or to body weight. The increase in weight was caused by fatty infiltration.

(3) Fatty liver was most common in the cases of kwashiorkor, but occurred sporadically in all the other groups. In the malnourished cases as a whole the amount of liver fat tended to be greatest in those which showed the least evidence of growth failure, as judged by weight and height.

(4) By comparison with a normal or ideal standard, the total amount of liver protein in the malnourished infants was reduced by nearly 40%. There was no significant difference in total liver protein between the cases of kwashiorkor and of marasmus. The greatest increase in liver fat was found in the cases with the least severe depletion of liver protein. This suggests that there is no causal connection between the 2 pathological processes— decrease in liver protein and increase in liver fat.

(5) There was a significant association between oedema and fatty liver. These are the 2 main diagnostic criteria of kwashiorkor in Jamaica.

(6) In the discussion 2 points are considered : the significance of the associations that have been found, and the nature of the distinction between kwashiorkor and marasmus.

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MATERNAL AND CHILD HEALTH SERVICES IN S.E. ASIA (IV) INDONESIA.

by

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Maternal and Child Health Centres.

The first (Chinese) infant welfare centre in the country was established in Djakarta — then Batavia — in 1930. By 1940 the number of centres in this city had risen to 10, and, since independence, MCH centres have been established all over the country, but mainly on the island of Java. There were 350 centres in 1951, 700 in 1952, 850 in 1953, nearly a thousand in 1954, 1355 at the end of 1955, and 1462 in June 1956. Of these 100 were in bigger towns, and the rest spread over most of the country, in 135 out of the 200 existing Regencies.

There is a rather unusual classification of centres in Indonesia into two groups : " reporting " and " non-reporting." This is explained by the fact that shortage of staff permits no, or little, supervision, so that information on activities is limited to reports.

Centres in rural areas are as a rule attended by midwives. One midwife is usually in charge of several centres, and conducts fortnightly clinics. In cities some centres are open two or three times a week and may have a few midwives on the staff, who are sometimes supervised by a doctor.

So far, the midwives are the backbone of maternal and child health activities, which are mostly limited to ante-natal care — mainly in the form of routine examinations—the distribution of milk, and, to a varying degree, domiciliary midwifery. Training of indigenous midwives is also part of the midwife's responsibilities. Although the centres are run by the Government, the midwives in charge are usually permitted to have private practice.

In some centres, the midwives are assisted by a type of worker, peculiar to Indonesia — the *Pengudjung rumah*, whose main responsibility is to follow up the midwife's advice by home visiting. They are, therefore, often called " home visitors " or " health visitors."

Table I, prepared by the Government, summarises the activities of the MCH centres.

Apart from the " ordinary " MCH centres, there are a few pilot projects. Unlike in most other countries in this region, there is no attempt to equip and staff such projects extravagantly, and in a manner which is out of all proportion to the usual services.

In Djakarta, a population of 250,000 (about 10% of the total) is served by the " Demonstration Hygiene Organisation". MCH work is included, and medical undergraduates visit the units for training purposes.

A Central Institute for Teaching and Research in MCH is being developed in Jogjakarta. So far there is only an out-patients clinic, and the training of assistant midwives. Eventually MCH centres, obstetric and pediatric wards, as well as a milk kitchen will be established. There is also an MCH demonstration area, near Jogjakarta with 4 centres, each staff with a midwife and a " home visitor."

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* I wish to thank Dr. Jacob de Haas and Dr. Georges Mettrop for unpublished material utilised in this review.

	1951	1952	1953	1954	1955
New visits to centres					
Women	16	19	25	28	33
Infants	9	12	16	19	23
Toddlers	5	8	9	12	16
Total visits to centres.					
Women	52	67	89	95	99
Infants	35	48	74	79	85
Toddlers	15	21	30	36	49
Home visits	—	26	34	44	49
Deliveries	5	5 - 6	6 - 7	7 - 8	7 - 8

TABLE I. Activities at M.C.H. centres in Indonesia (average figures per centre, per month).

In order to advise on the function of the MCH centres, an MCH Department was originally set up as a part of the Division to Combat Diseases at the Ministry of Health. Later — in 1952 — it was made a separate division, and transferred to Jogjakarta — 2 hours air travel from the capital. The staff consists of one medical and one administrative director, assisted by one medical officer and two midwives. In addition, one province so far — Mid-Java — has an MCH officer in supervisory capacity.

Regencies with a population of 3 - 600,000 have usually one doctor for all purposes, 4 - 7 midwives and a number of home visitors. One midwife delivers at the Regency hospital, the others work in one main and 3 - 4 sub-centres. Some of the Regency doctors attend clinics at the main centres. The municipal health service of Djakarta has an MCH officer, a pediatrician, and an obstetrician and a public health nurse on the staff.

Some views on infant nutrition in Indonesia can only be explained by the particular local pediatric tradition. Thus, for instance, acidified milk is universally advocated for artificial feeding, and early supplementary feeding is more often practised here than in neighbouring countries. There is a strong opinion that prolonged breast feeding is a major evil.

Milk kitchens are unusually popular, which is rather surprising in a country where milk is not a common element of the diet. Whatever the explanation, " milk - consciousness " is growing steadily despite experimentation with " non-milk protein foods."

SCHOOL HEALTH SERVICES

The first school health activities in the country were initiated in 1928 in Djakarta. Those are supervised by part-time general practitioners and male nurses. Since 1950 it became a part of the MCH service. A few of the other cities have similar set-ups, but the service is sometimes separate from MCH work.

The tendency is to train the teachers in health supervision, and make them responsible for most health activities in the schools. (15,000,000, that is about half of the school-age pulation in the country, actually attend schools). The usual procedure is for a team nurses and auxiliaries to visit each school once a year. The children are weighed, easured, vaccinated against small-pox, and often with BCG, and the sick are referred r treatment. In rural areas, this is being done by a single male nurse.

MATERNITY CARE

The tendency in the cities is, as anywhere else in the world, to take advantage of aternity hospitals. In Djakarta, there are, in addition to the two large obstetric hospitals ith 4,000 and 2,600 deliveries per year respectively, four municipal maternity homes and large number of small private maternity hospitals or homes.

Trained midwives operate mainly in cities and Regency headquarters. In Semerang, 5 - 80% of the deliveries are said to be conducted either in hospitals or by trained mid- ives. In the country as a whole, however, 95% of the total births are delivered by *dukums* indigenous midwives).

Some obstetric hospitals have large domiciliary services, for instance the Semarang Midwifery Hospital and School.

PEDIATRIC CARE AND PEDIATRIC TEACHING

Except for the teaching hospitals, specialised pediatric care is practically not yet available. There are altogether 5 pediatricians outside the island of Java. In Djakarta, the University Children's Department has 90 beds, and 40 beds for tuberculosis. A new building is being erected at present, and the total capacity will be 250 beds. Six pediatricians are on the staff, three of them working mainly in the out-patients' department, with a daily attendance of 500. New-born care is a pediatric responsibility.

In addition to the university department, there are in Djakarta children's wards at the Military Hospital and in three private hospitals. Other children's departments, one in Surabaya, Samarang (70 beds to be extended to 140) and in two hospitals in Jogjakarta. A 100-bed pediatric unit is being erected in Bandung. In the medical curriculum pediatrics is recognised as a major subject. The teaching consists of lectures, demonstrations and two months internship.

PERSONNEL

In 1954 there were 1,400 doctors in the country — 800 in government service. This means there was one doctor for 60,000 population in the Republic, one for 70,000 outside the capital city of Djakarta, and one for 200,000 outside the island of Java (population 54 million, out of the total of 82 million for the whole of Indonesia).

The number of obstetricians is estimated at between 20 and 30, and pediatricians between 15 and 20. Half of these specialists are in Djakarta. There are 4 medical colleges in the country: Djakarta, Surabaya, Jogjakarta and Medan.

Nurses are in short supply, and are utilised in hospitals only. Public health nurses are, so far, employed exclusively in an administrative capacity. A few have qualified abroad, but now a training course in Djakarta turns out 10 per year.

The number of midwives is 1,900 and about half of them are in government service. Two hundred, so far, had received a six-week refresher course in child care.

The traditional type of a trained midwife is the *bidan*, and some 1,200 of these work in the country. A *bidan* has six years primary schooling before she starts training as a *djurarawat* (assistant nurse). She then has 2 years practical experience, followed by two years midwifery training.

A new type of midwife is being trained at present as follows : 6 years primary school, 3 years high school, one years general nursing, and two years midwifery. 29 schools turn out 250 of these graduates annually, and 50% of them are supposed to be employed in institutions, and 50% in MCH centres.

In addition there are now seven schools for assistant midwives, with a total of 120 students, and a yearly output of 60. The minimum age of the candidate is 18 years, and they must have 6 years primary education. The curriculum consists of one years general education and nursing and two years midwifery, child care and public health. The number of graduates of all types of midwifery in 1955 was 243.

Pengudjung rumahs (home visitors) are now being trained in 6 schools. They are recruited mostly from rural areas, and candidates are also required to have 6 years primary education. The total number of students at present is 120. Their functions are : assisting midwives, health education, child care and giving advice in nutrition.

Dukuns (indigenous midwives) are being trained in institutions and MCH centres. The following table contains the number of *dukuns* trained or under training, as stated by the Government.

	1951	1952	1953	1954	1955
Under Training	329	1455	5739	5577	7032
Completed Training	—	135	1902	1103	1600

TABLE II. Training of *dukens* in Indonesia.

Vital Statistics. A birth and death registration system was introduced in 1933 with the help of Dr. HYDRICK. This was discontinued temporarily, and reintroduced in 1950 in Java. Data are usually collected by clerks, specially trained at the School of Statistics in Magolang.

The estimated mortality figures are as follows : general mortality 15 - 20 per thousand ; maternal mortality over 10 per thousand ; infant mortality 100 - 350 per thousand.

The maternal mortality rate in the large obstetric University Hospital in Djakarta is 4 per thousand, and, in another Djakarta Hospital attended by people of higher socio-economic status, it is only 3 per thousand.

Miscellaneous. Family planning is neither encouraged nor discouraged. The divorce rate is high. A social anthropologist who visited the country last year quotes statements by local authorities that in Java there is nearly one divorce to every two registered marriages. Fathers appear as a rule to retain custody of the children of the divorced wives.

A considerable amount of health education is done in Social Education Centres of the Ministry of Agriculture.

THE INCIDENCE OF SCARLET FEVER IN CURAÇAO (WITH A REPORT ON A DICK TEST SURVEY)

by

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Scarlet fever appears to be uncommon in the tropics, so that, while textbooks on this subject all make mention of sporadic cases, no epidemics have been observed (MANSON-BAHR, 1951 ; STRONG, 1945 ; GRADWOHL *et al*, 1951 and KOUWENAAR, *et al*, 1951). Reports from Indonesia were diffusely distributed over the entire Archipelago — Celebes, Java and Sumatra, and were concerned with isolated cases. According to STRANSKY and FELIX (1955), scarlet fever is unknown in the Philippines, and rare in Southern China. By contrast, SNAPPER (1941) remarks that it is endemic in the colder regions of North China. In India, scarlet fever is believed to occur and to have a benign course, although PHIPSON (quoted by RUGE, 1938) has described atypical fatal cases in Europeans in Bombay.

Scarlet fever has also been observed in Africa (e.g., Egypt, French Equatorial Africa and the Belgian Congo). MANSON-BAHR (1951) maintains that scarlet fever is seen sporadically in Africa, South America and the West Indies. KEAN (1946) has presented the results of a mortality survey in children up to the age of 10 years in the Isthmus of Panama zone — amongst whom were four fatal cases of scarlet fever, including three originating from the British West Indies.

In Curaçao small epidemics of such conditions as measles, mumps, whooping cough and sometimes poliomyelitis are a regular occurrence. Scarlet fever, however, is rare on the island. The senior author has seen a few sporadic cases in the course of 18 years' residence. For example, a ten-year-old boy was observed in 1941, showing a typical clinical course ; in 1951, a fatal case was observed in a 12-year-old girl, who was also suffering from diphtheria ; while in 1954 three further children showing the typical clinical picture were seen.

Acute rheumatic fever regularly occurs in Curaçao (HARTZ and VAN DER SAR, 1946). In previous publications we have expressed our surprise at the incongruence between the incidence of scarlet fever and that of rheumatic fever. In addition other streptococcal infections occur, including erysipelas, tonsillitis and streptococcal sepsis.

In Curaçao, as in other tropical and subtropical countries, the question is : " Why is scarlet fever so uncommon ? " Any approach to this question required a study of the immunity of the population concerned with the aid of the Dick test, which is still a reliable indicator in this respect. The Dick test was, therefore, carried out on 1,032 subjects of various age groups in the population of Curaçao, which is of mainly African ancestry.

CASE REPORTS

Case 1. A 12-year-old girl of African descent was admitted with acute laryngitis and a red rash. According to the mother, the child had become ill with a sore throat two days previously, followed two days later by redness of the face spreading over the entire body. The child was drowsy and swallowed with difficulty. On admission, the patient was drowsy, and the rectal temperature was 41.4°C. The throat was red and swollen, the tonsils being covered by a film which became blood-tinged when touched. The cervival lymph glands were markedly swollen. The heart and the lungs were normal, and the liver and the spleen were not palpable. The skin showed a typical scarlet fever eruption, together with purpuric spots in the inguinal region and on the elbows. The Rumpel-Leede test was positive. The child died eight hours later in spite of the administration of intravenous penicillin. Blood cultures were negative. Diphtheria bacilli and haemolytic streptococci were cultivated from the throat.

At autopsy, microscopic examination revealed accumulations of myocytes in the heart, but no characteristic Aschoff nodules. There was a separate leucocyte infiltration. The muscle fibres showed some degree of fatty degeneration. The liver showed fatty infiltration. There was some fatty infiltration of the renal tubules in the medulla, but not in the cortex. The skin showed oedema and haemorrhage in the papillae of the corium.

Case 2. A nine-year-old Negro boy was admitted with acute tonsillitis, possibly dihptheria. He had fallen ill two days previously, with a high temperature and a sore throat. He had not been inoculated against dipthheria. On examination, the boy gave the impression of being very ill. The tonsils showed marked swelling and atypical film. The tongue was furred. The cervical lymph glands were not swollen. The heart and lungs were normal, as were the abdominal organs. Neurological examination failed to reveal any changes. The temperature on admission was 38.2°C. The patient was given anti-diphtheria serum. The leucocyte count was 26,800 per c.mm. with 268 eosinophils per c.mm. Sickle cells negative ; Hb. 78% (12.2 g.). On the third day after admission, a typical scarlet fever exanthem developed, spreading over the entire body. The enanthem was also unmistakable, and a strawberry tongue was subsequently seen.

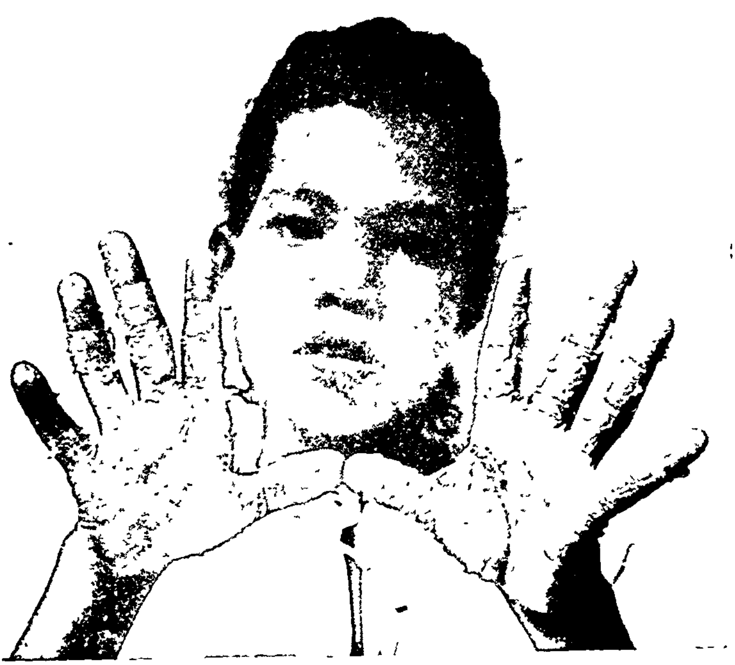

FIG. 1. 13-year-old Negro girl (Case 3) showing well-marked desquamation of both palms following scarlet fever.

The possibility of infectious mononucleosis was initially considered, but there was a negative Paul-Bunnell reaction. Both the cold agglutinin test and the Wasserman reaction were negative. Throat swabs were negative for diphtheria and streptococci ; haemolytic *M. pyogenes aureus* was demonstrated. Desquamation of the skin was seen, but was less typical than in case 3 There was a negative Rumpel-Leede test. In the third week after the outbreak of the rash the serum was tested for streptolysins, with the following results : antistreptolysin 80 units, strepto-L-agglutination 0 ; strepto-O-agglutination 1:160. The Rose test was negative. Serum obtained on the tenth day of the illness showed a typical Schultz-Charlton reaction. The further course was uneventful.

Case 3. A 13-year-old Negro girl was admitted to the St. Elisabeth Hospital with typical acute rheumatic fever. Temperature 40.8 C at admission and the throat slightly red. Throat swabs were positive for haemolytic streptococci sensitive to penicillin, chlortetracycline and chloramphenicol. Blood cultures were negative. The leucocyte count was 10,800 per c.mm. with a shift to the left. The sedimentation rate was 108 mm. for the first hour (Westergren).

On examination, mitral insufficiency was found in addition to the typical, painful swelling of joints of acute rheumatic fever. The ECG showed a prolonged P - R interval (0.22 second) with elevated and broadened P waves. On discharge the P - R interval was 0 18 second. The child was treated with cortisone and salicylates. A typical measles rash occurred on the 32nd day of illness ; the course was benign. On the 44th day of illness, the temperature suddenly rose considerably, and a typical scarlet fever exanthem and enanthem subsequently developed. Blood cultures were negative. A throat swab was negative for streptococci. There was no relapse of rheumatic symptoms. The temperature remained high for 10 days, and then came down by lysis.

On the 54th day of illness there were signs of jaundice. The Hymans Van Den Bergh reaction was 4.4 units (direct) and 0.9 units (indirect). Desquamation of the facial skin was seen on the 8th day after the development of the rash followed by typical large lamellar desquamations of the hands and feet 3 weeks later (Fig. 1). The Wassermann reaction was negative, as was the diazo-reaction. The Schultz-Charlton reaction with serum from Case 2 was positive.

Streptolysin determinations, on the 3rd day of the rash, showed the following results : antistreptolysin 100 units ; repeated 3 weeks later 250 units. Strepto-L-agglutination was negative on both occasions ; while the strepto-O-agglutination was positive (1 : 80), rising to 1 : 320 after 3 weeks. The Rose test was negative on both occasions. The further course was uneventful. The jaundice disappeared and the rheumatic signs disappeared.

Case 4. A Caucasian boy, aged 9, developed a scarlet fever rash which had still not completely disappeared 10 days later. There were no complications. Desquamation started on the 10th day—this was atypical with small sloughing patches No diphtheria or streptococci were cultured from the throat swab. The streptolysin titres 3 weeks after the outbreak of the rash were as follows : strepto-L-agglutination and Rose test negative , antistreptolysin titre 500 units ; strepto-O-agglutination positive (1 : 160).

Discussion

The case histories of these children show the typical course of scarlet fever, viz : tonsillitis, exanthem and desquamation. The streptolysin titres confirmed a streptococcal infection. Case 2 did not show a markedly positive titre, but her serum produced a typical Schultz-Charlton reaction in Case 3 at the height of the rash. A confusing finding was the M. pyogenes aureus culture from throat swabs in Case 2. Glanzmann (1952) has described a scarlatina-like rash in M. pyogenes aureus infections. Stevens (quoted by Glanzmann) observed three such cases, the Schultz-Charlton reaction was negative in these patients.

The Dick test results for the population of Curaçao, expressed in percentages, clearly shows considerable protective immunity even in the early age groups. The lowest immunity is found in the age group 5 - 15 years, with a peak at the age of 8 years (Fig. 2). The values obtained are considerably lower than the percentages given by Cooke (1927) for the U.S.A., which showed the minimal immunity to be found at the age of about 2 years (70 per cent. Dick positive). In the age groups between 6 and 20 years, Cooke's figure for the U.S.A. was 40 per cent. positive, whereas that for Curaçao is 18 per cent. —the difference is therefore in excess of 50 per cent.

Manson-Bahr (1951) states that in Tanganyika positive reactors were only one third as common as in Europe. The results of the Curaçao survey compare favourably with Indonesian values (Table).

Case Reports

Case 1. A 12-year-old girl of African descent was admitted with acute laryngitis and a red rash. According to the mother, the child had become ill with a sore throat two days previously, followed two days later by redness of the face spreading over the entire body. The child was drowsy and swallowed with difficulty. On admission, the patient was drowsy, and the rectal temperature was 41.4°C. The throat was red and swollen, the tonsils being covered by a film which became blood-tinged when touched. The cervival lymph glands were markedly swollen. The heart and the lungs were normal, and the liver and the spleen were not palpable. The skin showed a typical scarlet fever eruption, together with purpuric spots in the inguinal region and on the elbows. The Rumpel-Leede test was positive. The child died eight hours later in spite of the administration of intravenous penicillin. Blood cultures were negative. Diphtheria bacilli and haemolytic streptococci were cultivated from the throat.

At autopsy, microscopic examination revealed accumulations of myocytes in the heart, but no characteristic Aschoff nodules. There was a separate leucocyte infiltration. The muscle fibres showed some degree of fatty degeneration. The liver showed fatty infiltration. There was some fatty infiltration of the renal tubules in the medulla, but not in the cortex. The skin showed oedema and haemorrhage in the papillae of the corium.

Case 2. A nine-year-old Negro boy was admitted with acute tonsillitis, possibly dihptheria. He had fallen ill two days previously, with a high temperature and a sore throat. He had not been inoculated against dipthheria. On examination, the boy gave the impression of being very ill. The tonsils showed marked swelling and atypical film. The tongue was furred. The cervical lymph glands were not swollen. The heart and lungs were normal, as were the abdominal organs. Neurological examination failed to reveal any changes. The temperature on admission was 38.2°C. The patient was given anti-diphtheria serum. The leucocyte count was 26,800 per c.mm. with 268 eosinophils per c.mm. Sickle cells negative; Hb. 78% (12.2 g.). On the third day after admission, a typical scarlet fever exanthem developed, spreading over the entire body. The enanthem was also unmistakable, and a strawberry tongue was subsequently seen.

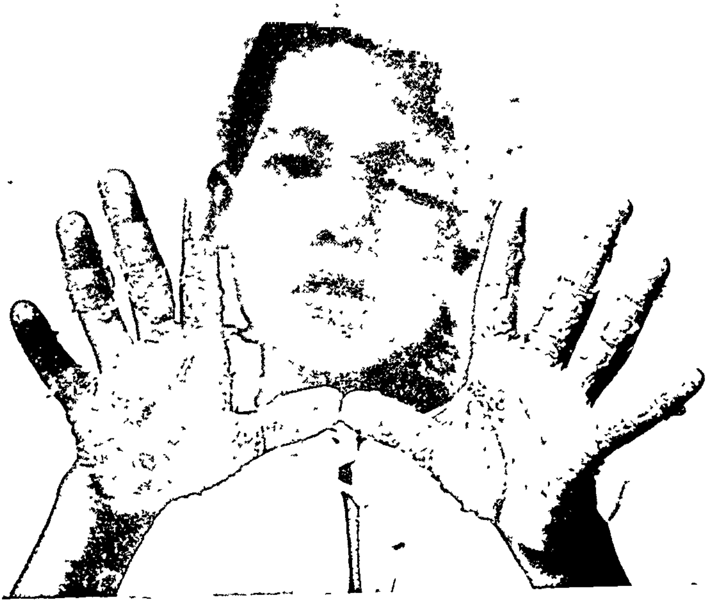

FIG. 1. 13-year-old Negro girl (Case 3) showing well-marked desquamation of both palms following scarlet fever.

The possibility of infectious mononucleosis was initially considered, but there was a negative Paul-Bunnell reaction. Both the cold agglutinin test and the Wasserman reaction were negative. Throat swabs were negative for diphtheria and streptococci : haemolytic *M. pyogenes aureus* was demonstrated. Desquamation of the skin was seen, but was less typical than in case 3. There was a negative Rumpel-Leede test. In the third week after the outbreak of the rash the serum was tested for streptolysins, with the following results : antistreptolysin 80 units, strepto-L-agglutination 0 ; strepto-O-agglutination 1:160. The Rose test was negative. Serum obtained on the tenth day of the illness showed a typical Schultz-Charlton reaction. The further course was uneventful.

Case 3. A 13-year-old Negro girl was admitted to the St. Elisabeth Hospital with typical acute rheumatic fever. Temperature 40.8°C at admission and the throat slightly red. Throat swabs were positive for haemolytic streptococci sensitive to penicillin, chlortetracycline and chloramphenicol. Blood cultures were negative. The leucocyte count was 10,800 per c.mm. with a shift to the left. The sedimentation rate was 108 mm. for the first hour (Westergren).

On examination, mitral insufficiency was found in addition to the typical, painful swelling of joints of acute rheumatic fever. The ECG showed a prolonged P - R interval (0.22 second) with elevated and flattened P waves. On discharge the P - R interval was 0.18 second. The child was treated with cortisone and salicylates. A typical measles rash occurred on the 32nd day of illness : the course was benign. On the [illegible] day of illness, the temperature suddenly rose considerably, and a typical scarlet fever exanthem and enanthem subsequently developed. Blood cultures were negative. A throat swab was negative for streptococci. There was no relapse of rheumatic symptoms. The temperature remained high for 10 days, and then came down by lysis.

On the 54th day of illness there were signs of jaundice. The Hymans Van Den Bergh reaction was 1.4 units (direct) and 0.9 units (indirect). Desquamation of the facial skin was seen on the 8th day after the development of the rash followed by typical large lamellar desquamations of the hands and feet 3 weeks later (Fig. 1). The Wassermann reaction was negative, as was the diazo-reaction. The Schultz-Charlton reaction with serum from Case 2 was positive.

Streptolysin determinations, on the 3rd day of the rash, showed the following results : antistreptolysin 100 units ; repeated 3 weeks later 250 units. Strepto-L-agglutination was negative on both occasions ; while the strepto-O-agglutination was positive (1 : 80), rising to 1 : 320 after 3 weeks. The Rose test was negative on both occasions. The further course was uneventful. The jaundice disappeared and the rheumatic signs disappeared.

Case 4. A Caucasian boy, aged 9, developed a scarlet fever rash which had still not completely disappeared 10 days later. There were no complications. Desquamation started on the 10th day — this was atypical with small sloughing patches. No diphtheria or streptococci were cultured from the throat swab. The streptolysin titres 3 weeks after the outbreak of the rash were as follows : strepto-L-agglutination and Rose test negative : antistreptolysin titre 500 units ; strepto-O-agglutination positive (1 : 160).

DISCUSSION

The case histories of these children show the typical course of scarlet fever, viz : tonsillitis, exanthem and desquamation. The streptolysin titres confirmed a streptococcal infection. Case 2 did not show a markedly positive titre, but her serum produced a typical Schultz-Charlton reaction in Case 3 at the height of the rash. A confusing finding was the M. pyogenes aureus culture from throat swabs in Case 2. GLANZMANN (1952) has described a scarlatina-like rash in M. pyogenes aureus infections. STEVENS (quoted by GLANZMANN) observed three such cases, the Schultz-Charlton reaction was negative in these patients.

The Dick test results for the population of Curaçao, expressed in percentages, clearly shows considerable protective immunity even in the early age groups. The lowest immunity is found in the age group 5 - 15 years, with a peak at the age of 8 years (Fig. 2). The values obtained are considerably lower than the percentages given by COOKE (1927) for the U.S.A., which showed the minimal immunity to be found at the age of about 2 years (70 per cent. Dick positive). In the age groups between 6 and 20 years, COOKE'S figure for the U.S.A. was 40 per cent. positive, whereas that for Curaçao is 18 per cent. — the difference is therefore in excess of 50 per cent.

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CASE REPORTS

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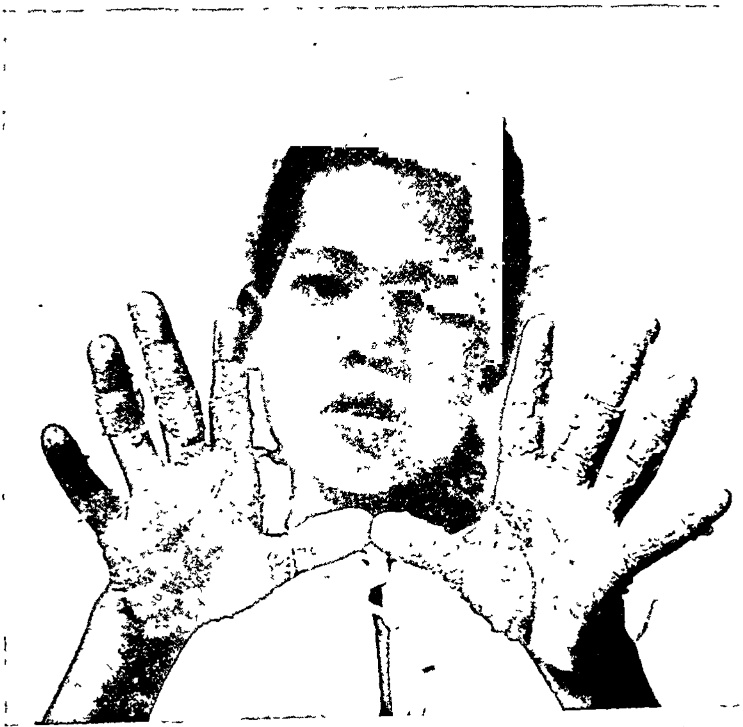

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Stransky and Felix (1951) used the Dick test on a limited scale in the Philippines, and their findings proved to be in close correspondence with those of Smits (1927) for Java. The number of tests made is too small, however, to warrant direct positive conclusions. In the Philippines Stransky maintains that positive reactions are no longer observed in adults ; similarly Curaçao there is almost complete immunity, from the third decade of life. Stransky explains the immunity of young babies as a result of immunity in adults, including mothers.

The conclusion is reached that immunity to scarlet fever in the tropics is attributable to latent infections undergone early in life. The same is suggested by the Curaçao curve as compared with the curve for Europe (Fig. 2). The explanation of this may be that other streptococcal infections induce immunity to scarlet fever or that an infection caused by scarlet fever streptococci here usually has a milder course (e.g. tonsillitis without a rash), as has been noted in some scarlet fever epidemics. The fact that haemolytic streptococci are regularly found in the throats at Curaçao is demonstrated by bacteriological findings. A haemolytic streptococcus was cultured from 15 per cent. of 188 throat swabs examined during the period May 1955, to January 1956 ; the same is suggested by the frequent occurrence of acute rheumatic fever at Curaçao.

The question : " Why is scarlet fever so uncommon in the tropics ? " can only be answered on the basis of exhaustive bacteriological investigations including determination of specific cultures, streptococcal titres and comparable Dick test surveys for larger groups of population.

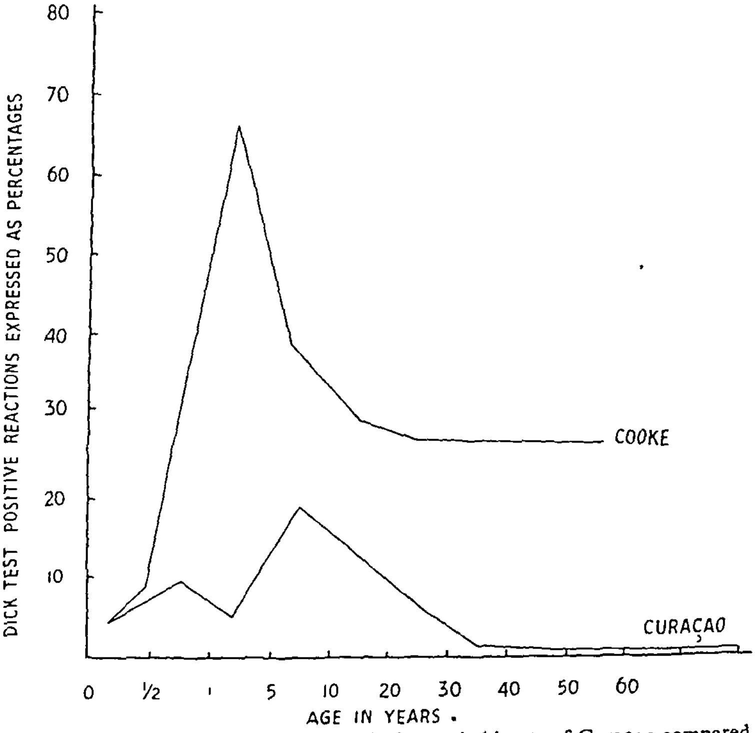

FIG. 2. Dick test in 1,032 predominantly African inhabitants of Curaçao compared with the figures of Cooke (U.S.A., 1927).

TABLE. Comparison of positive Dick reactions in different parts of the world.

Age (years)	Paris, Budapest, New York (1)	Yugoslavia (2)	Japan (3)	China (4)	Minahassa, Celebes (5)	Java (6)	Annam (7)	Philippines (8)	Curaçao (9)	U.S.A. (10)
0 - ½					50			11	3	4
½ - 1					100				8	32
1 - 3	35 - 70	85 - 97			90	70		81	4	68
4 - 5	40 - 65	62 - 92			60	27				63
6 - 10	30 - 50	20 - 72	43 - 68	21 - ?	50	25		10	17	39
11 - 15	26 - 38	19 - 39	22 - 36	15 - 22	56			0	12.5	30
16 - 20	20 - 26	14 - 20	11	11	66					
20 - 40					70	25	8	0		27

(1-5) quoted by Oomen, H. A. P. C. (1936). Gen. Tijdschr. voor Ned. Indië, 76, 2471.
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(7) Zoeller, Chr. (1924). C. R. Soc. Biol., 91, 1315.
(8) Stransky and Felix (1951). Ann. Paediatr., 177, 15.
(9) van der Sar.
(10) Cooke (cited by Glanzmann).

SUMMARY

The occurrence of a few cases of scarlet fever in children at Curaçao led the authors to conduct an immunity investigation among 1,032 Negro inhabitants with the aid of the Dick test. It was found that the population of Curaçao is highly immune to scarlet fever early in life. The lowest immunity was found in the age group 5 - 10 years. Comparisons are made with European values and those for other tropical countries, and the results are discussed.

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HERBAL MEDICINES AND DISEASE

by

R. SCHOENTAL*

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It is well known that technically underdeveloped countries, most of which are situated in the Tropics or Sub-tropics, present certain specific patterns in the incidence of diseases. Much progress has been made in recent years in the control of diseases of bacterial and parasitic origin. However, there are some other non-contagious diseases peculiar to these regions, the aetiology of which is unknown or uncertain, and which are responsible for much ill-health and high mortality in the communities concerned. In some of these diseases, particularly in those in which liver damage is the predominant feature such as kwashiorkor, liver cirrhosis and primary liver tumours, the use and abuse of particular medicinal herbs may be implicated.

Most medicines are potentially dangerous when used inappropriately or in excess and even after a full chemical, pharmacological and toxicological evaluation, fatal or disastrous consequences may follow drug treatment. For example, liver damage, even acute liver atrophy, may occur after treatment of syphilis with arsenicals ; poisoning of infants has followed the excessive use of teething powders containing mercury ; agranulocytosis is sometimes observed as a result of treatment with many drugs including some antibiotics. (REZNIKOFF and WELLS, 1956).

How much more risk may be involved in a treatment with crude medicinal herbs, of which the composition and content of the active principles may greatly fluctuate depending on the soil, the season and the climatic conditions.

Herbal medicines have been used since prehistoric times throughout the world. Until the 17th century, " Herbals " were the main books of materia medica, and they have left their mark at the present day in the Western Pharmacopoeias, which include a number of herbs of doubtful value under " vegetable simples " or " Galenicals." Many powerful and valuable drugs, like digitalis, quinine, morphine and others, had their origin in traditional herbal medicines. Many other of the folklore herbs, when subjected to scientific evaluation proved ineffectual or harmful, and have been, or are being, discarded from the medical armamentarium in civilised countries. In technically underdeveloped countries, however, the indiscriminate use of herbal concoctions continues to the present day.

It may be of interest to consider some of the rationale in herbal treatment. According to WECK (1937) in a Bali Pharmacopoeia, *Tarn premana* plants are classified according to the colour of their flowers and their taste. White, yellow or green flowers are considered as " warm," and so are sweet or sour plants. Red or blue flowers, bitter or spicy plants are " cold." When multi-coloured — they are " warm-cold " and so on. The treatment is based on opposites : against colds you take " warm " plants ; in fever you use " cold " ones. All plants which have a bitter or bad taste — are " cooling " for the stomach, while those which are sweet, sour or sharp are " warm."

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* I wish to thank Dr. C. D. Williams and Dr. J. M. Barnes for their interest and encouragement.

Other herbal systems (GRIEVE, 1931) rely on analogy and similarities ; plants with yellow flowers are used for jaundice, willows which grow in wet places are recommended for rheumatism, on the assumption that the latter is due to dampness. The shape of the plant, of its leaves and flowers, may also decide its application. Thus *Heliotropium* plants which have flower-stalks bent in a spiral have been recommended for snake and scorpion bites, because they resemble a snake's tongue.

JELLIFFE (1953) gives the following description of the treatment of infants by the Yoruba in Ibadan, Nigeria :

> " Following the ligature of the cord the child is bathed in a likewarm *herbal* bath and oiled. Its first feed consists of *agbo-omo*, an elaborate and variable decoction of *various herbs*, containing a mixture of barks, roots and dried leaves. This is force-fed until an appropriate degree of abdominal distention is produced, then the child is breast-fed. During the first few days of life *agbo* is given three times daily, before breast feeding. It is given as a general tonic, to ward off convulsions, as a laxative (some preparations are said to produce severe diarrhoea). It was suggested, without evidence, that it may contain an antimalarial constituent.
>
> If the mother dies, the baby is suckled by a relative or a neighbour. The African women induce artificial lactation by drinking *herbal* medicines, and by bathing the breast in a brew of mixed *herbs*, and then putting the baby on it." (Italics are mine).

WELBOURN reported from East Africa (1955) the same remarkable feature that the African women can induce lactation at any time in a foster mother, by the use of massage, herbs, warmth and suckling the baby. She quotes DAVIES (1950), who noted that the African women secrete large quantities of breast milk on a diet which is very poor in proteins without appearing to suffer any severe ill effects.

According to JELLIFFE (1953), the same is true for the Yoruba mothers in Western Nigeria who had adequate, even abundant, amounts of milk. The composition of the milk in the cases examined did not significantly differ from the milk of Caucasian mothers, and, although the quantity may decrease, its protein content did not fall off with the length of lactation. Among the Yoruba, breast-feeding is traditionally continued for 2 - 3 years, and longer.

In Tanganyika, according to NHONOLI (1954), a new born baby is not supposed to drink mother's colostrum, but is given a porridge prepared from medicinal roots by a family medicine man or woman, and some goat's or cow's milk. Only when flies settle on the mother's milk is this considered fit for the baby. The mothers after parturition also receive some medicinal roots to drink.

In this context it may be worth recalling that infant mortality in East and West Africa is still 300 - 500 per 1,000 live births, and that two-thirds of these cases often die during the first week of life (NHONOLI, 1954). In England the infant mortality is about 20 per 1,000 live births.

The position is well summarised by HARDING (1948) in a note on " Vital Statistics of a primitive peasant-tribe, the Kissi," in Sierra-Leone :

> " A high proportion of acute illness is attributed to witchcraft and recourse is had to native medicine men. Whatever the illness, native medicine is first tried, and it is usually only after an unsuccessful trial that the patient may, if still alive, be brought to hospital, often in an advanced condition."

During a recent visit to Israel, I had the opportunity of making inquiries about the use of herbal medicines among the unsophisticated new immigrants from neighbouring Arab countries (Iraq, Iran, Yemen, North Africa). All these communities brought to Israel their traditional customs, and the medicinal herbs of the countries of their origin, which they continue to use. While the young generation has been rapidly adopting the " western" way of life, the older people cling persistently to their traditions.

It appears that a great variety of herbs is still being used: Some are peculiar to only some communities, others are common to many. While the majority of herbal medicines are probably harmless, some may be less inocuous, while a few, among these, the plants containing the hepatotoxic Senecio alkaloids would be rather dangerous.

The name Senecio, used for denoting pyrrolizidine alkaloids has been to some extent misleading, as it seems to incriminate only plants of the genus Senecio. In a recent review, WARREN (1955) appropriately replaced it by the term pyrrolizidine alkaloids, in accordance with their chemical structure, consisting of hydroxymethyl-pyrrolizidine esterified by various branched-chain unsaturated or hydroxy-acids. Pyrrolizidine alkaloids have been isolated from many other genera, besides *Senecio*, including *Erechtites* (Compositae), *Heliotropium*, *Trichodesma*, *Trachelanthus* (Boraginaceae), *Crotalaria* (Leguminosae) and others. Only a few species of the various genera have so far been studied, but the increased interest in these alkaloids in recent years led to the elucidation of the chemical structure of several representative alkaloids, and to the synthesis of some products of their hydrolysis.

Plants containing these alkaloids have been traditionally used for the treatment of a great variety of disorders, such as colds, rheumatic pains, syphilis, impetigo and scabies, as laxatives, anthelmintics, emmenagogues and abortifacients, tonics and charms (CHOPRA, 1933 ; DALZIEL, 1937 ; DRAGENDORFF, 1898), and as constituents of the herbal infusions given to infants. Pyrrolizidine alkaloids can induce in experimental animals a variety of liver lesions, necrosis, fatty infiltration, fibrosis, hyperplasia and neoplasia (SAPEIKA, 1952 ; SCHOENTAL, 1955 ; SCHOENTAL, HEAD and PEACOCK, 1954 ; SCHOENTAL and HEAD, 1955). Unlike other alkaloids, which manifest their effects soon after the administration, these substances act insidiously, and appropriate dosage may allow the animal to survive for many months in apparent good health, before it ultimately succumbs to liver cirrhosis or liver cancer. One single dose may be enough to elicit various pathological conditions, depending on the length of time which elapsed between its administration and the death of the animal (SCHOENTAL and MAGEE*).

The various stages of the chain of pathological events elicited in experimental animals seem to correspond to some human diseases such as kwashiorkor, liver cirrhosis and primary liver tumours, in which liver damage is the main feature and which show particularly high incidence in technically underdeveloped countries.

The rôle of pyrrolizidine alkaloids in the aetiology of liver cirrhosis and primary liver tumours in technically underdeveloped countries is already gaining acceptance (BROCK, 1954a), but a suggestion that they may play a part also in the aetiology of kwashiorkor (SCHOENTAL, 1954) has met with criticism (BROCK, 1954b). It may therefore be worth recalling the present position of kwashiorkor and what is known about it.

Kwashiorkor is a syndrome which was first recognised and reported by CICELY D. WILLIAMS in 1933 among children in the Gold Coast. The name kwashiorkor means "the deprived child," in Ga, one of the languages of the Gold Coast, as it is supposed to occur in the child whose mother, while still breast feeding one baby, becomes pregnant again. The second child is thought to deprive the first one of its food. In the Gold Coast, as in many technically developing countries, breast feeding is usually continued till the child is 2-3 years old, or even longer. In some communities the woman is sent back to her parents and separated from her husband for the period of lactation. Thus to become pregnant during this time is to bear a stigma which the women would obviously try to avoid.

Since WILLIAMS' description of this condition, kwashiorkor has been reported from many parts of the world, including several African countries, India, Indonesia, Mexico, South America and even Italy, Spain and Greece in Europe. Kwashiorkor is not a clearly defined entity, and under its name have now been grouped various disorders, such as *Mehlnährschaden* etc., which are generally believed to be due to malnutrition. Kwashiorkor is primarily a disease of childhood, it occurs mainly between the 9th month and the 3rd year of life, but it has been described also in adults, mostly in women during pregnancy and lactation (TROWELL, DAVIES and DEAN, 1954).

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* These results have been communicated at a meeting of the Pathological Society of Great Britain and Ireland held in Manchester University on July 14th, 1956 (*J. Path. Bact.*, 72, 350, 1956) and have been submitted for publication in *J. Path. Bact.*

In children kwashiorkor is characterised by retarded growth, alteration of hair and skin pigmentation, oedema, usually associated with hypoalbuminaemia, dermatoses, gastro-intestinal disorders, peevishness and mental apathy, anaemia and high mortality. Pathological changes of the liver are always present, such as fatty infiltration, necrosis and fibrosis ; the pancreas sometimes shows atrophic or fibrotic changes and there is often a decrease of pancreatic enzymes. However, not all these characters are always present, dermatoses and the alteration of pigmentation of hair and skin, oedema, emaciation, fatty livers, anorexia are not constant features.

It is generally believed that this syndrome is due to protein deficiency, especially to the lack of first class animal proteins in the gruels given to children during weaning or to supplement the diminishing breast feeding. Since HIMSWORTH (1947) and others, produced experimentally a variety of liver changes by dietary deficiencies, it was natural to assume that the various liver disorders occurring in technically underdeveloped countries, including kwashiorkor, are due to malnutrition so prevalent in these areas. The reported success of skim-milk treatment of kwashiorkor seemed to support this view.

However, in the last few years, examples of kwashiorkor have been accumulating in children less than 1 year old and apparently adequately breast-fed (GELFAND, 1954 ; MACDOUGALL, 1954). To explain this, it was suggested that the mother's milk may be deficient in one or more essential factors (BROCK and AUTRET, 1952). There is, however, no evidence that this is the case ; the milk of African mothers compares favourably in protein content with that of Caucasian mothers (JELLIFFE, 1955). Although skim-milk is effective in reducing fatty infiltration of the liver, some doubts have been expressed as to whether the " initial " cure observed in some cases is an " actual " one (GALVAN, 1955). Even with skim-milk treatment, the mortality in kwashiorkor is still 20% and more.

In recent years, the world-wide problem of kwashiorkor has received much attention and has been the subject of special inquiries made on behalf of the World Health Organisation by BROCK and AUTRET (1952) in Africa, and by AUTRET and BEHAR (1955), in South America.

In all considerations of the problem of kwashiorkor there has not been any enquiry into the herbal medicines given to the affected babies or possibly used by the mothers during the time which elapsed between the conception and the onset of the child's illness. In some unsophisticated communities, the drugs intended for the infants are given to the women who suckle them (WECK, 1937).

It seems significant that there is sometimes a high incidence of kwashiorkor cases among children of women who, from various reasons, may be suspected of having used some emmenagogue or abortifacient preparations. Thus :

> " In Curaçao 55 per cent. of kwashiorkor patients are in children of unmarried mothers. The same holds good for Fiji, even in women who disobeyed the tribal law that pregnancy must be avoided when the child is on the breast. In the West Indies and Africa, a number of cases come from homes where there are seven or eight other children " (MANSON-BAHR, 1954).

In her first publication on this problem WILLIAMS (1933) remarked that her cases occurred in children whose mother " was dead, or has become pregnant again while the patient was still young, or the mother has been ill or undernourished."

She also noted :

> " When a woman dies in child-birth or soon after, the surviving baby is generally adopted by the maternal grandmother and breast-fed by her, possibly with the help of her sisters and other daughters. These foster-children usually die early. It is not a question of the survival of the fittest, but the survival of just a few of the luckiest. In former days an infant that survived its mother was looked upon by the Ashanti people as a bad "ju-ju" and was invariably destroyed. Among the Ga and Fanti and the Coast tribes this is not so, but they believe that the spirit of the dead mother comes back and poisons the child's food, and finally persuades the spirit of the child to follow hers."

From this description, it is evident that milk treatment, e.g., suckling the baby by foster mothers, has been tried by the African villagers themselves, and that they come to realise that there is no help for such children, and that sooner or later these will die.

Admittedly it may not be easy to obtain the necessary information from the mothers as to the composition of the preparations which they have used, e.g., in order to prevent pregnancy during lactation. The distrust of the scientific doctor may not be the only reason for their reticence :

> " The natives are sometimes frightened to death of the witch-doctors. The *modus operandi* is to curse the devoted one, prophesying his early death, etc. The victim generally gives up hope and dies on the very day named. Of course poison is often secretly administered along with the curses, but some cases are beyond a reasonable doubt, mere fright." (Wellman, 1904).

Liver cirrhosis is by no means a purely tropical disease. It is fairly common in the U.S.A. and still more so in France, where it is believed to be of alcoholic origin. There is however a fundamental difference in respect to age incidence of this disorder between the technically underdeveloped and the Western Countries. While in France, for example, the incidence increases rapidly after the age of 50 years, or so, in underdeveloped countries, high incidence is encountered among young people and children. No adequate statistical data are available from these countries, where dead are often buried without the knowledge of the authorities. Data taken from the Epidemiological and Vital Statistics of the WHO for Trinidad and Tobago, and for Israel (1953) may serve as an illustration (Table).

Table. Incidence of liver cirrhosis per 100,000 population (average for males and females).

		Age groups in years						
Country.	Year	- 1	1-4	5-9	30-34	55-59	60-64	All ages
United Kingdom	1952	1.6	0.1	0.2	0.4	6.0	7.6	2.6
France	1951	0.7	0.1	0.1	2.9	97.7	114.4	24.3
Israel	1953	11.1	6.2	1.4	1.9	15.0	16.0	4.1
Trinidad and Tobago	1953	8.7	4.7	2.3	6.2	28.9	31.2	5.8

This high incidence of infantile cirrhosis of the liver in Israel in 1953 coincided with the admission of unsophisticated immigrants from several Arab countries (Yemen, Iraq, North Africa, etc.) It was not observed among the Jews from Europe, before the influx of these " oriental " Jews, as they are known locally. Indeed, when I visited Israel last year, the cases of infantile liver cirrhosis shown to me in various hospitals were all in children of " oriental " parents.

Data published for some Arab countries where, on religious grounds, liver cirrhosis cannot be alcoholic give a similar picture. Thus, Stacey (1944) reported that it is common among children and especially frequent among the poor *fellaheen* (farm labourers) of from 30-40 years old. Yenikomshian (1934) published some figures for Lebanon and Syria, and compared these with the incidence of liver cirrhosis in New York. While in New York the incidence is 13 per cent. below 40 years of age and 5 per cent below 20 ; in the countries mentioned 63 per cent. are below 40, and 20 per cent below 20 years of age. In New York 45 per cent. were in alcoholics; in Syria only 9 per cent.

A toxic factor has often been suspected by many authors, who like VINT (1931), have suggested that it may be derived from food or from intestinal helminths, but no specific substances have been identified. Malaria, parasitic infestation and malnutrition prevalent in these countries have all been suggested and may no doubt be involved in the high incidence of the various liver disorders. In ill-health one resorts to medicines, and when the latter contain injurious agents a vicious circle may be set up. The more illness — the more medicines; the more medicines — the more irreversible the damage, especially when malnutrition makes the individual more vulnerable to the action of toxic agents (DRILL, 1942).

Primary liver tumours. This type of tumour (in contradistinction to metastatic liver involvement) is very rare in Western countries where it constitutes less than 1% of all the cancer cases. However, in some communities in Africa it may represent up to 80 per cent. of all the cancer cases.

Age incidence of this condition is again significant. While in the Western world it is a disease of old age among the Africans, young people, even children may be affected. The available statistical data were mainly collected among young men, e.g., among the workers in gold mines in Johannesburg (BERMAN, 1950) or among soldiers in West Africa during the last war, whose average age was 25 years (FINDLAY, 1950). Among the latter the incidence of primary hepatic tumours was 61.6 per cent. of all the cancer cases.

Although many factors associated with poverty, ignorance and malnutrition must play a part in producing these liver diseases, there seems to be reasonable grounds for suspecting hepatotoxic substances present in herbal medicines of playing a rôle.

Suspicion has become attached to the Senecio alkaloids because of their ability in many animal species to produce liver lesions of a wide variety of pathological types.

Recent observations in this laboratory have shown that a single dose of Senecio alkaloids given to young rats may produce severe liver damage which can be seen at the death of the animal, which may occur several months later, thus suggesting that herbal medicines forced down a baby's throat in early life might reveal their effects as kwashiorkor, or, several years later as a fully developed liver cirrhosis perhaps associated with primary liver tumours.

Animal experiments in a problem like this may only suggest possible leads in elucidating the cause of a disease such as kwashiorkor. Any rôle played by herbal medicines can only be established by collecting more data on the general use of herbal remedies and some exact knowledge of the composition of those in common use. Such information can only be collected by field studies, though the toxicity or otherwise of the plants may be tested by administration to experimental animals, of which the rat seems to be the species of choice. Identification of the effective chemical constituents can then be attempted.

SUMMARY

It is suggested that the extensive use of medicinal herbs in the tropics and sub-stropics may have a bearing on the incidence of some diseases peculiar to these regions. In particular, such diseases as kwashiorkor, liver cirrhosis and primary liver tumours, in which the liver is primarily involved, may be related to the ingestion of plants, such as those containing pyrrolizidine (Senecio) alkaloids. Various liver lesions, including fatty infiltration, fibrosis, hyperplasia and neoplasia have been observed in experimental animals as a result of treatment with these alkaloids, administered many months before the onset of illness.

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A NOTE OF THE TREATMENT OF KWASHIORKOR

by

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At the Gambia Conference in 1952, we gave an account of the methods we were then using for the treatment of kwashiorkor (DEAN, 1954).

Amongst the details that seemed important, we included the necessity to offer about 50 g. protein daily, and to restrict the amount of sugar, including the lactose of dried milk, because of the danger of causing diarrhoea. We pointed out also that the fat of the soya bean appeared to be well tolerated.

We have repeatedly observed that recovery is most rapid in those children in whom a high caloric intake can be established without delay, and there are good theoretical grounds for believing that the synthesis of new protein — obviously desirable if we believe that kwashiorkor results in protein depletion — is accelerated by the presence of ample calories.

In the circumstances, it seemed reasonable to try to incorporate in our therapeutic diets either soya oil or other vegetable oils of similar fatty acid composition. Soya oil is not available locally, but there is a large local production of a cottonseed oil of high quality that is used widely for cooking purposes. We have found that it can safely be given, in amounts of 30 g. or more daily, in the acute stage of the disease, and causes neither vomiting nor diarrhoea. We have continued to use calcium caseinate as the chief source of protein, and to restrict the amount of sugar, but we add the cottonseed oil to the other ingredients by mixing in a high-speed electric blender. The oil is not homogenised, but is finely divided. When the feed is allowed to stand for some hours, a film of oil appears on the surface, but can be dispersed by stirring. The dispersion is helped by heating, and most children seem to prefer the feeds warm. Some details of mixtures in which the oil is incorporated are given in the Table. As a rule, 4 to 5 feeds are offered daily, each of 200 to 250 g., but the only restriction on intake is the child's appetite. In accordance with usual pediatric practice, the feeds are diluted with an equal amount of water, or given in smaller quantities and at more frequent intervals, if there is any tendency to vomiting.

In balance studies, we have found that 15 to 20 per cent. of the oil may escape absorption, and the real caloric gain is therefore somewhat less than the theoretical caloric value of the food. Nevertheless, the rate of improvement in the clinical condition of the children and in their blood chemistry has been excellent, even in those severely ill with advanced skin lesions, much oedema and a very poor appetite. The stools do not look as though they contain fat.

The composition of diets suitable for children at different stages are shown in the Table. With these diets, a caloric intake exceeding 100 kg. body weight can usually be achieved within the first days of treatment, and as soon as oedema has been lost, the weight gains should be good.

TABLE. Diets used by the Medical Research Council's Infantile Malnutrition Group, Kampala, for the treatment of kwashiorkor.

	Ingredients. (g.)						Value of 100 g. mixture (g.)		
	Calcium caseinate	Dried skimmed milk	Sugar	*Oil*	Water	Calories	Protein	Fat	CHO
For a fairly severe case	50	50	20	30	850	70	5.7	3.0	4.5
For a very severe case	50	0	20	30	900	53	4.0	3.0	2.0
with much diarrhoea	75	25	20	30	850	70	6.7	3.0	2.0
For a convalescent child	0	120	20	30	830	75	4.1	3.0	8.0
	0	120	20	50	810	93	5.0	5.0	8.0

Preparation.

The dried skimmed milk is made into a paste with cold water, and hot water is then added, and brought to the boil with constant stirring. The sugar and oil are added, and the mixture is put into a high-speed electric blender. The volume is made up to 1 litre.

The possession of a diet that is entirely bland, and is known not to cause diarrhoea, is a valuable asset because it often happens in acute kwashiorkor that there is a diarrhoea whose cause is uncertain. A diarrhoea persisting whilst a bland diet is being given can, we believe, be regarded as infective in origin, or the accompaniment of an infection, although it may be impossible to discover any pathogenic organism.

The mixtures containing the oil have been under trial for nearly a year and in that time have been given to about 80 children. One child, who was very severely ill at the age of a year and is being kept in hospital to try to ensure his attaining the full height and weight of a healthy child of his age, has had one or other of the mixtures every day for nine months and is thriving excellently.

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PROTEIN AND FAT BALANCE STUDIES IN CHILDREN RECOVERING FROM KWASHIORKOR*

by

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The clinical, biochemical and physiological characteristics of kwashiorkor have received wide-spread attention, and have been the subject of several reviews (TROWELL, 1954 , *Conference on protein malnutrition*, 1953 , SCRIMSHAW et al , 1956) However, most studies have been confined to the acute and initial recovery stages of the syndrome Despite the fact that the successul rehabilitation of children with kwashiorkor requires long and costly hospital treatment, little information is available on the metabolic characteristics of children in the late stages of recovery.

The amount of protein and fat and the number of calories per kilogram of body weight which will produce optimal recovery are also uncertain. Furthermore, there is little information as to how much the diarrhoea, which the child recovering from malnutrition frequently acquires in an open pediatric ward, affects recovery.

HOLEMANS and LAMBRECHTS (1955) have studied the nitrogen retention of children recovering from kwashiorkor on daily protein intakes ranging from 0 5 to 7 8 gm per kg of body weight and found that within this range the amount of nitrogen retained increases with the amount of protein fed GÓMEZ et al (1956) have reported a linear relationship in children with kwashiorkor between the amount of protein consumed and both the nitrogen absorbed and retained within a range of 2 2 to 4 1 gm. per kg. of milk protein However, absorption and retention of nitrogen were both relatively poor on similar children fed corn and beans GÓMEZ et al (1956) have also reported the absorption of fat to be reduced in such cases but to improve steadily as recovery occurs. The only data on children in the late recovery phase are those of DEAN (1953) who reports the absorption of nitrogen and fat in three cases to be still somewhat reduced.

The present paper presents the results of 12 periods of metabolic study in four children who were in the stage of late recovery, or what is referred to by BROCK et al. (1955) as " consolidation of cure " Although more cases must be studied in order to resolve the uncertainties mentioned, the data reported are already helping to improve the management of our patients with kwashiorkor and provide suggestions of value for public health programmes directed toward the prevention of protein malnutrition.

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* Assisted by Grant in-aid No A-981 from the National Institute of Arthritis and Metabolic Diseases of the United States Public Health Service, and by funds from the World Health Organization and the Williams-Waterman Fund of the Research Corporation

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MATERIAL

Four children were admitted to the hospital with moderate or severe kwashiorkor. In each case their signs and symptoms included growth retardation, oedema, apathy and anorexia, skin and hair changes and diarrhoea. Biochemical findings included lowered blood serum protein and albumin and reduced activity of serum amylase, pseudo-cholinesterase and alkaline phosphatase. They had completed initial recovery on a mixed diet high in milk protein and were gaining weight at the time that the metabolic balance studies were begun. Other pertinent clinical data for each case can be summarized as follows :

F.A., a boy aged 2 years and 7 months, was admitted with severe kwashiorkor 10 weeks before the first balance period. He had been hospitalized for the same condition one year previously. On admission he weighed 9 8 kg. and dropped to 7.0 kg. with the loss of oedema. His height was 77.5 c.m.

F.C., a boy aged 8 years and 11 months, was admitted with moderately severe kwashiorkor 6 weeks before the first balance period. His weight on admission was 18.3 kg. and dropped to 12.1 kg. with the loss of oedema. His height was 104 cm.

T.A., a boy aged 1 year and 5 months, was admitted with severe kwashiorkor of a pronounced marasmic type 6 weeks before the first balance period. On admission his weight was 7.4 kg. and dropped to 5.6 kg. when all oedema was lost. The child was still thin and gaining weight slowly when the metabolic studies were begun. His stools were semi-formed and numbered 5-6 per day. He developed bulky stools during the first balance period but these improved during the second and his rate of weight gain increased. Presumably, due to the drastic drop in the amount of protein given to him, his weight decreased during the adaptation period preceding the third balance trial, but remained stable from 3 days before the trial was actually begun until the experiment ended.

R.L., a girl aged 5 years and 11 months, was admitted 4 weeks before her first balance period with mild kwashiorkor of long standing. Her initial weight was 14 kg. but dropped to 11.6 kg. when her oedema was lost. Her weight was 100.5 cm. Her recovery was clinically and biochemically well advanced at the time of the first trial period and her clinical recuperation was considered complete 8 weeks after admission.

METHODS

In order to insure complete collection of urine and faeces during each five-day balance period, the two older children were closely supervised and the two younger ones strapped in a specially adapted bed. The urine was collected under toluene in flasks surrounded by ice. Faeces were collected in a small pot and subsequently washed with distilled water into a glass jar. Both urine and faeces were refrigerated or frozen daily until the collection was completed and the analyses could be done on the composite 5-day sample. One hundred mg. of carmine were administered with the first meal of the period and the collection begun when the dye appeared in the faeces. Five days later an equal amount of carmine was given and the collection of faeces terminated when red stained stools appeared.

The diet ingredients were weighed with an accuracy of 0.1 gm. and a one-tenth aliquot of each food set aside in the refrigerator for subsequent analyses. Nitrogen was determined in the diet, urine and faeces samples by the Kjeldahl method (Hamilton and Simpson, 1946) and fat by that recommended by the A.O.A.C. (1950).

The dietary intakes of protein and calories were designed to meet specific levels considered desirable for the study. The food composition values obtained by INCAP (1953) were used for these calculations which, in general, agreed well with the analytic values for the whole diet. Caloric adjustments were made by varying the quantities of sugar, corn starch and fat included in the diet. During the period of the metabolic studies all children received a vitamin mixture daily which supplied : Vitamin A, 5,000 I.U. ; Vitamin D, 1,000 I.U. ; Thiamine HCl, 1.5 mg. ; Riboflavin, 1.2 mg. ; Niacin, 10 mg. ; Ascorbic acid, 50 mg. ; Pyridoxine HCl, 0.5 mg.

The nitrogen absorbed was calculated as equal to the nitrogen intake minus the nitrogen excreted in the faeces. The nitrogen retained was assumed to be the quantity absorbed less that excreted in the urine. In accordance with Macy (1942) and Allison (1955), but in contrast to Holemans and Lambrechts (1955), no correction for faecal nitrogen was made in calculating the nitrogen absorbed.

RESULTS

The amount of protein, fat and calories consumed per kg., the amount of protein per 100 cal. and the body weight and clinical status in each period are shown in Table I together with the data on nitrogen and fat absorption and nitrogen retention. When recovery was progressing satisfactorily, the absorption of nitrogen was high but the retention varied from 16.4 to 52.9 per cent. The milligrams of nitrogen per kilo actually retained ranged from 95 to 259. Under the same circumstances the percentage of fat absorbed varied from 31.9 to 88.5 per cent.

TABLE I. Metabolic data in children recovering from kwashiorkor.

Patient	Weight in kg.	Clinical status	Principal Protein source	Dietary Intake				Nitrogen			Fat % Abs.
				Protein		Fat	Cal.	Abs.	Retained		
				gm./kg.	gm./100 Cal.	gm./kg.	kg.	%	%	mg./kg./day	
R.L.	12.7	Good recovery	Acid whole milk[1]	2.9	2.2	1.9	130	78.4	44.0	205	88.5
R.L.	14.3	Good recovery	Skimmed milk[2]	3.1	2.6	0.8	115	85.5	52.9	259	71.3
F.A.	9.6	Good recovery	Acid whole milk[1]	5.3	3.7	3.6	144	79.8	27.7	240	78.0
		Diarrhoea 1 day						13.5	-1.0	-6	60.8
F.A.	9.8		Skimmed milk[2]	3.8	3.1	1.0	122				
		Post ,, 4 days						57.5	4.6	28	59.6
F.A.	10.4	Slightly bulky stools	Skimmed milk[3]	4.0	3.5	0.7	115	75.1	17.3	112	31.9
F.A.	10.8	Good recovery	Skimmed milk[3]	4.1	3.6	1.3	114	81.5	23.1	150	77.5
F.A.	11.2	Good recovery	Skimmed milk[2]	2.6	2.4	0.9	108	74.1	23.0	95	52.9
T.A.	7.1	Bulky stools	Half sk. milk[4]	7.3	5.4	1.8	135	75.1	11.7	137	87.2
T.A.	7.4	Slightly bulky stools	Skimmed milk[2]	9.4	7.1	0.9	132	84.2	16.4	247	57.8
T.A.	7.5	Stationary weight	Skimmed milk[2]	2.6	2.6	0.4	99	86.6	3.2	13	77.6
F.C.	14.6	Good recovery	Skimmed milk[2]	6.2	5.8	0.8	106	82.2	14.0	138	78.7

1. " Pelargon "—Supplied by Nestlé Co. 2. Supplied by UNICEF. 3. " Golden State." 4. " Nesbrum "—Supplied by Nestlé Co.

The balance period in F.A., in whom diarrhoea occurred during the first day, followed by relatively loose bulky stools for the remaining four days, showed a very marked adverse effect of the diarrhoea on both the absorption and retention of nitrogen. The former dropped from 79.8 to 13.5 per cent. in the first day and returned only to 57.5 per cent. in the following four days. The latter dropped from 27.7 per cent. to a negative 1 per cent. and returned only to 4.6 per cent.

There was a general tendency for the amount of nitrogen and fat absorbed per kg. per day to increase linearly with the amounts fed. This is illustrated for nitrogen in Fig. 1 and for fat in Fig. 2. These figures include the linear regression equation and line for each correlation. The percentage of nitrogen retained showed great variation from one child to another. There was no tendency for the amount of nitrogen retained per kg. per day, to show a correlation with either the amount of nitrogen consumed or absorbed. The relationship between the amount of fat consumed and that absorbed was highly variable. Unlike the absorption of nitrogen, the absorption of fat does not appear to be affected by a period of diarrhoea.

DISCUSSION

When no diarrhoea was present, the percentage of nitrogen absorbed by these children was remarkably uniform and the average value of 80.2 per cent. is probably a good indication of the amount of absorption to be anticipated under the circumstances of these trials. This average is less than the 90 per cent. given by MACY (1942) for well nourished children. Our figure may indicate a slight impairment of absorption even late in recovery.

Surprisingly, the average per cent. absorption of nitrogen in the present study is almost the same as that reported by HOLEMANS and LAMBRECHTS (1955) for 28 balance periods in children with acute kwashiorkor. In view of the evidence that gastrointestinal enzymes are drastically reduced in acute kwashiorkor (TROWELL et al., 1954 ; *Conference on protein malnutrition*, 1953 ; THOMPSON and TROWELL, 1952 ; and GÓMEZ et al., 1954), this would confirm a very rapid recovery of the proteolytic enzymes (VEGHELYI, 1948) before the child could be placed on the metabolic trial. From the standpoint of practical therapy it means that the large quantities of protein customarily administered in the treatment of kwashiorkor are digested and the nitrogen absorbed. A very rapid recovery has also been noted for serum protein and albumin and for several of the serum enzymes (TROWELL et al., 1954 ; SCRIMSHAW et al., 1956).

The percentage of absorbed nitrogen retained by the body may be expected to show a great deal more variation. When the quality of protein is constant the most important cause of this variation will be the degree of depletion of body stores. In early recovery the retention may be expected to be relatively large, but this is bound to decrease as the tissue needs are met and normal balance is approached. On the other hand, the percentage of nitrogen retained at the stage when tissue deficits have been satisfied will depend upon the total amount of nitrogen absorbed and the rate of growth.

The question should be asked, however, whether or not the feeding of very high levels of protein in recovery actually results in more nitrogen being retained by the body or simply causes an increased urinary and faecal nitrogen excretion. The figures obtained together with those of HOLEMANS and LAMBRECHTS (1955) and GÓMEZ et al. (1956) suggest that there is an essentially linear relationship between the amount of nitrogen fed and the amount retained per kg. per day, as long as the body is depleted of protein. However, this no longer applies to children who have been fully repleted of protein and who have

(1956) regarding the effect of the vaccination upon acutely exposed adolescent girls in a school in Denmark, and with the study Dahlström and Difs (1956) of BCG-vaccination in the Swedish army during the war. I suppose that it might be said, that there is a rather unanimous agreement among those who have had experience with this prophylactic procedure ; an adequately made BCG-vaccination, that is, a vaccination that has had time to produce tuberculin sensitivity before exposure, undoubtedly provides fairly satisfactory protection against the immediate consequences of a tuberculous infection, against serious forms of primary tuberculosis, against the early postprimary diseases, miliary tuberculosis and tuberculous meningitis, as well as against pleurisy and early postprimary pulmonary tuberculosis. The protection against late postprimary types of tuberculosis seems to be slighter and more uncertain.

What has been said about the efficiency of BCG-vaccination may also be applied to the use of the vole bacillus as an immunizing agent, according to the experience of the British Medical Research Council (1956). There seems to be no reason to change over from BCG to the vole vaccine.

At present there are some other problems regarding BCG-vaccination that are more generally discussed, namely the duration of the immunity, the use of freeze-dried vaccine, the untoward effects of the vaccination and the general principles of the vaccination as a public health measure.

Regarding the first question, that of *the persistence of the immunity*, it is not possible to arrive at any definite conclusions, and we here meet another problem, that of the method of assessment of immunity. Usually the existence of immunity is measured by tuberculin tests. We must admit, however, that tuberculin sensitivity and specific immunity are not identical. Lacking other easily applied methods of assessment, we have to rely upon the tuberculin sensitivity, when we want to determine the existence of immunity. Another factor that may interfere is the occurrence of subclinical tuberculous infection, which may influence the persistence of the immunity. With these reservations in mind, it might be said that the immunity can disappear within one year, but on the other hand, according to our experience, it can last for as long as 7 - 10 years or perhaps more. The duration of the immunity thus varies considerably — and it is not possible in advance to tell how long it will last. In all events it will as a rule last sufficiently long to be of real benefit to an exposed child.

Regarding *the use of lyophilizied BCG*, there are without doubt some advantages to be gained through facilitating storage and distribution of the vaccine and also making its potency more uniform. Researches now in progress have shown thus far that freeze-dried vaccine may be used effectively up to one year after production, but with a certain decrease of its potency. At present it would be premature to recommend its general use, at least in countries without transport difficulties.

In countries with a well developed public health service and very low tuberculosis morbidity rate, *vaccination of selected groups* of the population, especially those who run an evident risk of exposure, seems to be the principle of choice — if there is any need of vaccination at all. Such selected groups are family contacts, medical students, student nurses etc. In countries with a very high tuberculosis morbidity rate, the risk of exposure is very great and thus there is need of more *general vaccination*. The latter principle has been followed by the World Health Organisation (1954) in its campaign against tuberculosis in post-war Europe and in its present campaign in Eastern countries. Usually, when BCG-vaccination is introduced into a country where there is no previous experience of its efficiency, it is at first tentatively given to selected groups of the population. After its benefit has been demonstrated, it is extended to larger and larger groups. This seems to be a logical development of the vaccination in a country with high tuberculosis morbidity rate. The reverse development, diminishing the use of general vaccination and continuing with vaccination of only selected groups when the tuberculosis morbidity rate has decreased to a very low figure, should be logical too. When only a few percent. of children become infected at 15 years of age, as in Sweden, there seems to be little indication to continue with general vaccination, for instance, of newborns. Although the resistance is lowest in early infancy, the risk of exposure is so small that there is little need of vaccination of this age group. If a more general vaccination should be performed in such a country the policy recommended by the British Medical Research Council (1956) seems to be that which should be preferred, i.e. vaccination fo school-children at pre-puberty age.

Many reports have been published of *complications or untoward reactions* after BCG-vaccination. These reactions are usually local and have developed at the site of the administration of the vaccine, and in the regional lymphatic glands in the form of abscesses. Lymph-node abscesses are always to be regarded as abnormal reactions, but local skin abscesses only when they are large and persist for a long time. The incidence of such complications in adequately performed vaccinations varies considerably with the commercial origin of the vaccine used, with the dose and the mode of administration and with the degree of susceptibility of the child. We have had very little trouble in this respect with intradermal administration of an adequate dose of the Swedish vaccine.

In addition to these untoward local reactions there are a few reports on the development of lupus in the neighbourhood if the site of the vaccination.

Some words may be added about the occurrence of *systemic BCG-processes.* During the last 5 years a few cases of such an abnormal course of BCG-vaccination have been published from the Scandinavian countries. These cases have been carefully studied and, according to my opinion, it must be admitted that BCG-bacilli in extremely rare instances may give rise to chronic inflammatory processes by haematogenous spread of the bacilli. These cases have not been due to a too-potent vaccine, because the same sample has been used in other children without any complication at all, nor do they depend upon an error in the administration of the vaccine. It is probably unknown individual factors, causing an abnormal susceptibility, that are responsible. In relation to the many hundred thousands of vaccinations performed in Scandinavia and the great protective benefit derived from these vaccinations, the occurrence of such an abnormal susceptibility is extremely rare and its significance should not be exaggerated.

In *conclusion* it might be said that tuberculosis in infancy and childhood may be prevented by the application of general public health measures aiming at the enlightment of the population, satisfactory milk hygiene, control of the health of people who have professional contact with children and by adequately performed BCG-vaccination.

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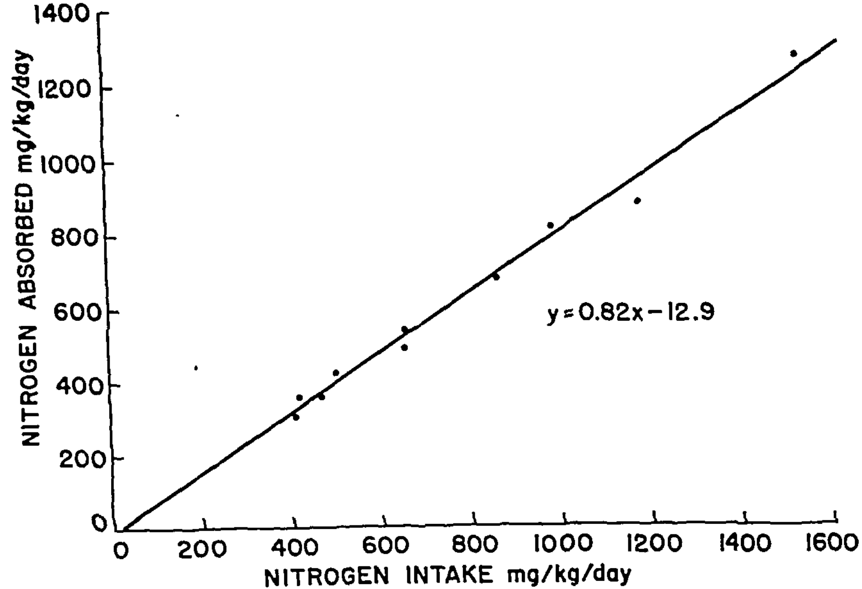
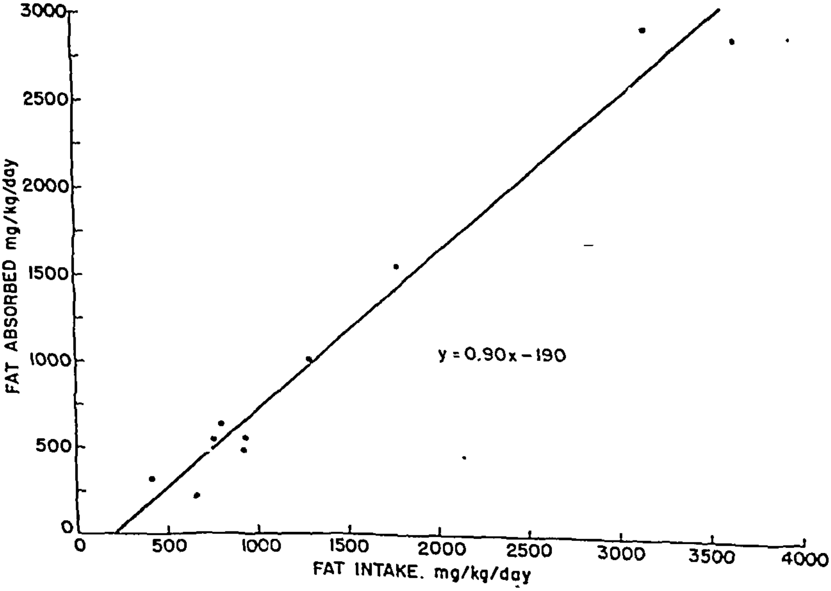


INCAP-1956

FIG. 1. Relationship between nitrogen intake and nitrogen absorption in children recovering from kwashiorkor.



INCAP-1956

FIG. 2. Relationship between fat intake and fat absorption in children recovering from kwashiorkor.

regained the appropriate weight for their height. This would explain why R.L. retained 259 mg. of nitrogen per kg. per day on an intake of only 3.1 gm. per kg., while F.C. retained only 138 mg. on an intake of 6.2 gm. of protein per kg., even though the protein came from skim milk in each case.

The data appear to justify relatively high protein intakes for therapy during the active recovery period. In fact, the case of T.A. illustrates the danger of not maintaining a high enough protein intake. This child was showing excellent clinical progress and weight gain at the beginning of the balance studies. When given 7.3 gm. of protein per kg. he retained 137 mg. per kilo and when this was increased to 9.4 gm. his retention increased to 247 mg. per kilo. However, when his intake was reduced to 2.6 gm. per kg. he was barely able to maintain a positive nitrogen balance and weight gain not only stopped, but his weight stayed stationary as long as the protein intake was held at this relatively low level.

It is of great interest that the child with diarrhoea neither absorbed nor retained nitrogen well, although a one-day balance is subject to a relatively large experimental error. Additional studies of children with diarrhoea are obviously indicated. The data presented support the suggestion that diarrhoea may be a very important factor in the original development of acute kwashiorkor (AUTRET and BÉHAR, 1954 ; SCRIMSHAW et al., 1955) and in the relatively slow recovery of cases in open pediatric wards where infections producing diarrhoea are common (SCRIMSHAW et al., 1956). This may be due in part to the drop in duodenal enzymes reported by VEGHELYI (1948) for children with infectious diarrhoea.

Neither acid whole milk, nor half skimmed milk appeared to have any advantage over skimmed milk, although too few cases were involved for conclusions on this point. As would be expected, the degree of recovery of the child was more significant in determining the nitrogen retention than the number of weeks in the hospital. Too few cases were studied to allow comments on the effect of either the age or the weight of the child on the values cited. Since the children were not studied metabolically until recovery was deemed satisfactory, it is not likely that severity of the kwashiorkor entered importantly into the trials.

The factors responsible for the relatively large variation in the amount of fat absorbed are not readily apparent. In general, the percentage of ingested fat absorbed was considerably less than the 97 per cent. for normal children given by MACY or 90-95 per cent. cited by DOCHAIN and LAMBRECHTS (1954). It was also lower than that reported by HOLEMANS and LAMBRECHTS (1955) for acute kwashiorkor, but higher than in most of the cases studied by GÓMEZ et al. (1956). It should be noted that the determination of fat absorption was only an incidental part of the study and most of the fat intakes were relatively low. Only additional studies can indicate the value or adverse effect of higher fat intakes in the treatment of kwashiorkor. From the present study, it does not appear that the amount of fat present in whole acid milk is less readily handled by the child than the small amount of fat in the skimmed milk.

SUMMARY

The nitrogen absorption and retention of four children recovering from acute kwashiorkor of the marasmic type were determined in twelve metabolic balance periods begun after initial recovery. When milk protein was given in amounts varying from 2.6 to 9.4 gm. per kg., nitrogen absorption in uncomplicated kwashiorkor varied from 74.1

to 85 5 per cent., with an average of 80 2 per cent. The nitrogen retained per kg per day showed no correlation with the protein intake or absorption Both nitrogen absorption and retention were drastically reduced by an episode of diarrhoea. A daily level of 2 6 gm. of protein per kg. was barely sufficient for positive nitrogen balance in a boy 18 months of age and did not support growth The fat intakes ranged from 0.4 to 3 6 gm per kg per day and the fat absorbed showed a positive linear correlation with the amount fed.

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PROPHYLAXIS OF TUBERCULOSIS IN CHILDHOOD*

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Prevention of tuberculosis in childhood includes two objectives, prevention of infection and prevention of the development of tuberculous disease from the infecting bacilli. By prevention of infection the children are, of course, protected in the most efficient way against tuberculosis. If there is no tuberculous infection, there can be no tuberculous disease. To protect children from infection, however, is often very difficult. even if all available public health measures are applied. These measures include a satisfactory milk hygiene and control of the health of people who have professionally to do with children. In countries with a very high tuberculosis morbidity rate, the sources of infection are so numerous that almost no children escape infection. In countries with a moderate morbidity rate about half of the children become infected, while in countries with a very low mortality rate, such as in Scandinavia, only a few children run the risk of exposure, and the prevention of infection is therefore an easier task.

Once tuberculous infection has occurred it depends largely upon the resistance of the child whether tuberculous disease will be manifested. If the resistance is high, no disease will occur, while, if the resistance is low, the child may die from tuberculosis. The factors that determine the degree of resistance may be divided into two groups: non-specific and specific. The non-specific, natural resistance depends upon the age of the child when infected and upon genetic, constitutional and environmental factors. The specific resistance is due to immunity conferred by a previous infection. It has long been known that a tuberculous infection produces an increased specific resistance against subsequent infections. This immunity is without doubt of benefit to the child, but at the same time the bacilli producing the immunity may constitute a potential danger, threatening the child with tuberculous diseases of various kinds. Therefore it was a great advance when Calmette and Guerin managed to produce their BCG-strain of tubercle bacilli and showed that it could be used as an immunizing agent.

Many reports have been published which intend to show the efficiency of BCG-vaccination, but most of them are presented in such a way that their frequently very optimistic conclusions seem unwarranted. I will only quote a few of those which I regard as being reliable. The most recent study and, according to my opinion the best planned one, is that performed by the British Medical Research Council (1956). It concerns about 25,000 tuberculin-negative adolescent school-children, chosen at random, living in an ordinary environment, half of them were BCG-vaccinated, the other half having been left unvaccinated as controls. The two groups were subsequently examined carefully at regular intervals. A preliminary report was published when the study had run for 2½ years. It was found that roughly 5 times as many clinical cases of tuberculosis had occurred in the unvaccinated group as in the vaccinated one. Of special interest is the fact that there were 6 cases of miliary tuberculosis and tuberculous meningitis in the unvaccinated group, as against no case in the vaccinated children. The report concludes that the *BCG-vaccination had produced a substantial protection against tuberculosis.*

The result of this study corresponds fairly well with the experiences reported by ARONSON (1952) of vaccination among American Indians in U.S.A., with those of HYGE

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* Report read at the VIIIth International Congress of Pediatrics, Copenhagen, July 1956.